This is a digital copy of a book that was preserved for generations on library shelves before it was carefully scanned by Google as part of a project to make the world's books discoverable online.

It has survived long enough for the copyright to expire and the book to enter the public domain. A public domain book is one that was never subject to copyright or whose legal copyright term has expired. Whether a book is in the public domain may vary country to country. Public domain books are our gateways to the past, representing a wealth of history, culture and knowledge that's often difficult to discover.

Marks, notations and other marginalia present in the original volume will appear in this file - a reminder of this book's long journey from the publisher to a library and finally to you.

Usage guidelines

Google is proud to partner with libraries to digitize public domain materials and make them widely accessible. Public domain books belong to the public and we are merely their custodians. Nevertheless, this work is expensive, so in order to keep providing this resource, we have taken steps to prevent abuse by commercial parties, including placing technical restrictions on automated querying.

We also ask that you:

+ *Make non-commercial use of the files* We designed Google Book Search for use by individuals, and we request that you use these files for personal, non-commercial purposes.

+ *Refrain from automated querying* Do not send automated queries of any sort to Google's system: If you are conducting research on machine translation, optical character recognition or other areas where access to a large amount of text is helpful, please contact us. We encourage the use of public domain materials for these purposes and may be able to help.

+ *Maintain attribution* The Google "watermark" you see on each file is essential for informing people about this project and helping them find additional materials through Google Book Search. Please do not remove it.

+ *Keep it legal* Whatever your use, remember that you are responsible for ensuring that what you are doing is legal. Do not assume that just because we believe a book is in the public domain for users in the United States, that the work is also in the public domain for users in other countries. Whether a book is still in copyright varies from country to country, and we can't offer guidance on whether any specific use of any specific book is allowed. Please do not assume that a book's appearance in Google Book Search means it can be used in any manner anywhere in the world. Copyright infringement liability can be quite severe.

About Google Book Search

Google's mission is to organize the world's information and to make it universally accessible and useful. Google Book Search helps readers discover the world's books while helping authors and publishers reach new audiences. You can search through the full text of this book on the web at `http://books.google.com/`

LANE MEDICAL LIBRARY STANFORD
2 45 0174 1858

Sulphate of Quinine

Manson

With the
Compliments
of the Autho

LANE

MEDICAL LIBRARY

SEAL OF THE LELAND STANFORD JUNIOR UNIVERSITY
SEMPER VIRENS
1885

LEVI COOPER LANE FUND

With the
Compliments
of the Autho

A TREATISE

ON THE

PHYSIOLOGICAL AND THERAPEUTIC ACTION

LANE LIBRARY

OF THE

SULPHATE OF QUININE.

BY

OTIS FREDERICK MANSON, M.D.,

PROFESSOR OF PHYSIOLOGY AND PATHOLOGY IN THE MEDICAL COLLEGE OF VIRGINIA.

LANE MEDICAL LIBRARY
14833
SAN FRANCISCO

THE PROPERTY OF THE NEW YORK HOSPITAL
NOV
14
189

PHILADELPHIA:
J. B. LIPPINCOTT & CO.
1882.

Copyright, 1882, by J. B. LIPPINCOTT & Co.

.C53M2
1882

THE PHYSIOLOGICAL AND THERAPEUTIC ACTION

OF THE

SULPHATE OF QUININE.

Although nearly two-thirds of a century has elapsed since the introduction of quinine into the materia medica, yet perhaps there is no agent in its vast catalogue concerning whose properties such opposite opinions are held, or which has elicited more discussion. When we reflect on the facts that its employment has been co-extensive with that numerous class of diseases known as Periodical Fevers and the protean maladies considered as arising from the same cause, and that it has been the subject of experiment and study among the most distinguished physicians of the age, it is a matter of surprise that no positive and generally recognized opinion should have been established in regard to its powers, properties, and method of employment. Certainly an agent whose effects upon the organism are so prompt and conspicuous must have some definite mode of action, and surely a remedy whose transcendent virtues are the theme of almost universal praise must possess a remarkable degree of certainty in its effects, and if potent for good cannot be altogether harmless when untimely and injudiciously exhibited. Believing that this apparently irreconcilable diversity of views, in regard to its properties and *modus operandi*, has arisen from imperfect or limited observation, and in many cases from the bias of preconceived opinions, we think that the time has arrived when some definite conclusions can be formed on the subject. Facts, numerous and well attested, are before us, and, with a conscientious desire to develop the truth, it shall be our endeavor to examine them impartially and to deduce from them correct conclusions and safe and salutary practical results.

HISTORY.

Early in the present century the attention of practical chemists was directed to the analysis of several vegetable remedies, and among these the various species of cinchona were the subject of investigation. Already morphine, strychnine, and veratrine had been discovered, but no satisfactory analysis[*] of cinchona had been made until the year 1820, when MM. Pelletier and Caventou, Parisian chemists, succeeded, after protracted and laborious experiments, in discovering the salifiable base, which they termed *kinine.* Experiments were immediately made with it on animals by M. Magendie, and by MM. Double, Villerme, and Chomel, on patients affected with intermittent fever, and by M. Renauldin[†] in remittents. Its employment became rapidly extended throughout Italy, England, and Germany. "In 1822, Professor Mathias,[‡] in thirty-one cases of simple and double-tertian intermittents, effected cures by giving the sulphate of quinine, in quantities of from fifteen to thirty-five grains, in two or three days. This gentleman also reported two cases of remittent; the one cured by bark and the other by the sulphate of quinine.

---

[*] We are aware that Dr. Gomez, of Lisbon, had previously discovered cinchonine in an impure state.

[†] M. Renauldin communicated the first fact of this nature, and shortly after M. Magendie (in his *Journal de Physiol.*, July, 1821), himself, had an opportunity of administering the same medicine with success. *Vide* Magendie's Formulary, American edition, Phila., 1834, p. 52.

[‡] Magendie's Formulary (from *Giornale Arcadico di Roma*, Noumbre, 1822), page 53.

M. Rossi treated sixty-four persons laboring under intermittents, of different types and species, by means of sulphate of quinine; eight tertians, twenty-nine double-tertians, two quartans, twenty-seven sub-continued, and eight remittents were cured. Fifty patients had no attack after the first dose; seven had them in a slight degree. The quantity administered varied from twelve to seventy-two grains, but in twenty-four cases it was not necessary to go beyond twenty-four grains. M. Tonelli also relates that sixty-five cases of intermittent were cured, with the exception of one, which was in a hopeless state when the remedy was resorted to. Of these, four were quotidian, twenty-two tertian, thirty-one double-tertian, three quartans, two double-quartans, two sub-continued, and one remittent. Forty-two patients never had a return of the paroxysm after the first dose. The quantity given to each varied from twelve to eighteen grains. In 1823, Dr. Giacomazzi, of Brescia,* Tommassini, and others also employed it, and found its effects to correspond with those of the bark. In the July number of the *Philadelphia*

---

* Traité de Matière Médicale et Thérapeutique, par G. A. Giacomini, Professeur de Médecine Clinique à l'Université de Padoue, traduit par Mogon et Rognetta, Paris, 1839, p. 349.

Journal of Foreign Medical Science and Literature (vol. ii. p. 498, 1822) appeared a review of the "Analyse Chimique des Quinquinas, par MM. Pelletier et Caventou (à Paris, 1821)," and the "Formulaire pour la Préparation et l'Emploi de plusieurs Nouveaux Médicamens, par F. Magendie (à Paris, 1821)," in which the principal facts in regard to the discovery, employment, and effects of the sulphate of quinine were stated. Soon after articles from different sources appeared in the American medical journals, and its use rapidly became general.

The discovery of quinine was hailed by the profession in both hemispheres with enthusiastic delight. The objections to the bark, on account of its bulk, its bitter, nauseous taste, and its liability to produce vomiting and diarrhœa, were now obviated by the substitution of a light powder, which could be administered with facility, and whose ordinary dose at that period could be given in a pill. The distinguished chemists, to whom the profession and humanity itself became so signally indebted, received the plaudits of the civilized world, and must forever be entitled to the gratitude of mankind.

The introduction of the new alkaloid was soon destined to revive the controversy which had existed for more than a century in regard to the properties of the Peruvian bark, of which it was considered the substitute and representative. It is well known to the scholar that, since the time of Morton,* the most opposite views were held on the subject of the employment of the bark in special conditions of the system, and in regard to its use in various diseases. By many—we may say by the large majority of writers—cinchona had been regarded as the first and most valuable of *tonics*, possessing excitant and stimulant properties, which rendered its use hazardous in the presence of fever and inflammation; whilst on the other hand, in the opinion of a numerous and powerful minority, it was held to be endowed with sedative and even antiphlogistic virtues in the same conditions of the organism. The controversy has therefore been renewed in our day, with as much zeal and earnestness as in the famous discussion between Ramazzini † and Torti ‡ in the past century.

---

* Opera Medica, Lugduni, 1737.

† Opera Omnia, Genevæ, 1717 (De Abusu Chinà Chinà, p. 218–238.

‡ Therapeutice, Specialis, ad Febres Periodicas Perniciosas, Leodii, 1712.

Happily, however, at present we possess facilities for the elucidation of the vexed question denied to those illustrious disputants. The advance of science has cast aside many obstacles in our path, and the improved methods of investigation of the present age, and the accumulation of facts derived from the observations and experiments of more than a hundred years, must necessarily afford the most useful aid towards the solution of the problem.

ACTION OF QUININE.

We propose, then, to follow the methods usually resorted to to determine the effect of medicine, by investigating: 1st. *Its action on animals;* 2d. *Its effects on man in health;* and 3d. *Its effects on the human organism in disease.*

1. **Action on Animals.**—Although we are compelled to dissent from the declaration of Magendie, that "medicines and poisons act in the same manner on men as on animals,"* yet numerous experiments lead us to the belief that the sulphate of quinine produces effects on the human organism very closely allied to the phenomena observed when administered to brutes.

---

* Magendie's Formulary, Preface to the 6th Amer. Edition.

The first experiments recorded were made by M. Magendie himself;* and he states that he at once perceived that it "possessed no poisonous property, and, indeed, manifested no immediate action whatever;" yet we are not informed in what quantities it was administered, or how numerous were his trials of the article. M. Briquet,† however, is of the opinion that the quantity administered did not exceed *one gramme*,‡ and that the examinations of the animals were not carefully made.

In 1840, M. Giacomini, a professor in the University of Padua, instituted a series of experiments on rabbits to demonstrate the views of the Italian school in regard to the *hyposthenisant* § properties of quinine. Of fifteen rabbits, to whom he administered, on an average, twenty-three grains each, with one gramme of alcohol, six recovered, three died, and six perished accidentally in the course of the experiments. Of eleven rabbits, to whom were given eighteen grains of sulphate of quinine, with four grammes of distilled water, ten died immediately, and only one recovered. All of these animals were agitated, tottered in their gait, experienced slight convulsive movements, followed by extreme prostration and debility. After death, the veins of the pia mater and the large veins of the thorax were found distended with black blood; the lungs of a roseate tint, and the mucous membrane of the alimentary canal of a normal color. These experiments were repeated by MM. Saudri, Balardini, Ludi, and Bergnoni with similar results.*

---

* Magendie's Formulary, ed. cit., p. 50.

† Traité Thérapeutique du Quinquina et de ses Préparations, 2d ed., p. 21.

‡ A French gramme is equivalent to fifteen and two-fifths grains of troy weight.

§ Term given by the Rasorists to agents which depressed the vital powers.

In 1843, Dr. F. Mêlier read before the French Royal Academy of Medicine a paper containing his "Expériences et Observations sur les Propriétés Toxiques de Sulfate de Quinine,"† in which were related several experiments on dogs with that salt. As this paper has attracted considerable attention, we translate the only two experiments which were given in detail.

First Experiment.—Thirty-one grains of sulphate of quinine mixed with a small quantity of water were introduced into the stomach of a young healthy dog, of medium size, *the œsophagus being tied.* After six minutes efforts to vomit, expulsion of thick, white mucus from the bronchi. After thirty minutes the efforts to vomit ceased; general trembling; indisposition to move; dilated pupils; pulse 135 per minute. After six hours, state of debility; general trembling; animal sad; respiration normal. After fifteen hours, respiration difficult; coma and insensibility. After twenty hours, animal lies on the side, convulsive movements, *subsultus tendinum;* stertorous respiration; death at the end of twenty-two hours.

---

* Briquet, op. cit., p. 43.

† Mémoires de l'Académie Royale de Médecine, x. 722.

Autopsy.—Sanguineous congestion of the pulmonary tissue; several portions of the lung of a blackish-brown color and hepatized; sank in water, whilst the remaining portions floated. Brain congested and its veins and arteries distended. The blood drawn from the vein at the moment of death remained fluid, or at least only formed a soft diffluent clot, resembling a species of jelly.

SECOND EXPERIMENT.—Forty-six grains of *acid* sulphate of quinine were introduced into the stomach of a healthy dog of medium size, who had eaten an hour before. The œsophagus tied. After fifteen minutes, violent efforts to vomit;

copious expulsion of bronchial mucus. After an hour, general trembling; titubation; indisposition to move. After *eight* hours, condition the same; pulse 160 per minute; efforts to vomit ceased; tendency to repose, convulsive movements of the head; respiration very difficult. After twenty hours, death.

Autopsy.—Cerebral and pulmonary congestion. Congestion of the mucous membrane of the stomach; blood black and incoagulable. The urine, tested with iodide of potassium, gave a precipitate indicating the presence of quinine. The serum of the blood did not present this precipitate.

These experiments, which were repeated by M. Mêlier, were intended to ascertain the toxicological effects of quinine and the manner in which it produced death. They are evidently very imperfect, and do not justify the conclusion that the ordinary effect of quinine in large doses is to produce liquefaction of the blood and acceleration of the pulse. It is true that the salt given in such quantities as to paralyze the nervous system must be followed by corresponding depression of the action of the heart and arteries; and in this state of debility, the heart doubtless acted with greater frequency. But this is merely the characteristic condition of extreme depression, by whatever means it may have been produced. A pulse of extreme frequency is the invariable accompaniment of extreme debility, as well as the usual harbinger of dissolution. Nor does the apparent congestion of the cerebral and pulmonary vessels prove that death resulted therefrom. They were evidently passive congestions, arising from paralysis of the vessels. We shall show hereafter that quinine, so far from producing directly either congestion of the brain or lungs, is one of the most certain agents for the removal of those conditions.

It now becomes our pleasant task to notice the experiments of M. Briquet in his "Traité Thérapeutique du Quinquina," a work which, for its extent and research, deserves the highest commendation. Although holding opinions ourselves diametrically opposite to his on some important points, yet we take pleasure in stating our conviction that the vast array of facts and carefully-conducted experiments found in his work has given a notable upward impulse to the science of therapeutics, and must produce the most valuable practical results. We shall be compelled, not only from a sense of duty, but also from necessity, to quote his work frequently, as it contains information to be derived from no other source. At present, however, his experiments on animals particularly demand our attention.

This sagacious observer essayed a large number of experiments upon dogs, and first endeavored to ascertain the modifications produced by quinine on the circulation. By means of the *hémodynamomètre* of M. Poiseuille (an instrument invented to denote varying degrees of the force of the arterial current), he proved that the salt injected into the jugular vein in the direction of the heart of the animal, produced a depressing influence on the circulation. In six experiments, when the quantities of the salt varied from seven to thirty grains, the strength of the arterial current was reduced to one-tenth and to one-fourth of its normal force. In the thirteenth experiment, in which thirty-one grains were injected, death was suddenly produced. In the eighth experiment, twenty-six grains were used with fatal effects, at some period of the night. M. Briquet concluded from these and further experiments,—

1. That the sulphate of quinine injected into the veins towards the heart in sufficient quantities immediately suspends the action of that organ.

2. That this suspension produces death by a

veritable syncope, resulting from an annihilation of the contractile power of the heart; for, in the first place, the suspension of the contractions of the heart is so sudden, and the loss of contractility so complete, that after death we find the left cavities of the heart and the aorta itself filled with scarlet blood, which is never observed in ordinary deaths; and in the second place, the heart laid bare exhibited only very slight vermicular movements, very different from those precipitate and energetic movements observed in animals who have quickly died in other kinds of experiments. Lastly, the lungs were invariably found of light, rosy hue, as soft as eider-down, and without the least trace of engorgement.

3. That the rapidity of death and the extent of the diminution of the contractility of the heart was in direct ratio to the quantity of the salt injected.

4. That animals offer very different degrees of resistance to the destructive power of quinine according to their strength. Thus, in the first five experiments in which the animals were vigorous and in good condition, thirty grains were necessary to produce the same results which doses of eight to fifteen grains produced in those who were small, thin, and feeble.

5. That the influence of quinine on the circulation is felt at least *twenty-four hours after* its introduction into the animal economy, and may *continue several days.*

6. That the relative proportion of fibrin in the blood was always augmented when a large quantity of the sulphate was administered, and diminished when it was discontinued.

7. That the relative proportion of blood-globules was diminished by the action of quinine.

8. That the serum of the blood was increased after its administration, but that this result, as well as the diminution of the globules, was due in part to the privation of food to which the animals were necessarily subjected during and after the experimentation.

Action on the Brain.—In the experiments just noticed, made to determine the action of quinine upon the circulation and on the blood, its effects on the brain were also incidentally noted.

When quantities varying from fifteen to thirty grains were injected, the animals became restless, were affected with slight convulsions, subsultus tendinum, and tottered in their gait. But M. Briquet desiring to test more perfectly the effect of the salt on the encephalon, instead of injecting the medicine in the direction of the heart, through the jugular vein, injected the salt into the aorta, when immediately the animals became agitated, trembled, endeavored to escape, and clung with all their strength to the ground. Their eyes became bright and animated, the respiration and circulation were accelerated, and they exhibited extreme titubation. In two cases convulsions occurred. This ensemble evidently constituted a period of excitation of brief duration.

In a few moments after two of these experiments, and at the end of four hours in two others, the agitation ceased; the animals lay down and were disinclined to move, or moved very slowly when forced to stir; the respiration became slow, the pulse small, and the skin cold.

The *diminution* in the *force* of the *arterial circulation* measured by the hémodynamomètre was shown in a *very evident manner*, in the *majority* of cases in this stage.

This condition continued until the recovery or death of the animal, and constituted a second period in which phenomena of *sedation* were conspicuous, and always continued a much greater length of time than the period of excitement. The effect of quinine when injected in the direction of the heart was observed to be much greater than when injected in the direction of the brain. From these experiments M. Briquet drew the following conclusions:

1. That the sulphate of quinine acting directly on the encephalon presents in this action a first period, in which is exhibited clearly an excitement of that organ, but that this period is of brief duration and the effects of *moderate* degree.

2. That in the *second* period, which occurs *promptly*, and endures for a *long time*, signs of *sedation* are manifested, which, from their degree and importance, constitute, in a manner, the *veritable action of the agent.*

3. That the brain resists the sedative action of the salt with more energy than the heart.

4. That in cases where the introduction of the sulphate of quinine is effected *slowly* and *gradually*, *no phenomena* of *excitation* are observed; the animals only present titubation, *debility*, *torpor, and disinclination for exertion;* then the steps are slow, uncertain, and vacillating; their feet are separated far apart to enlarge the base of sustentation; they appear stupefied, and their pupils are greatly dilated.

5. That this action of quinine is purely dynamic,

and only attains to the degree of inflammation in rare cases where its action has been too energetic or too direct.

6. When the injections of quinine are made into the *femoral artery*, *the pleura*, *and the cellular tissue*, the same series of symptoms were always seen *except those of the period of excitation*, the period of *sedation only having been present*.

Action on Man in Health.—The effects of the sulphate of quinine on the human subject in health have been frequently observed, and resemble very closely those manifested in animals. M. Magendie informs us in his "Formulary"* that M. Caventou, being obliged to taste this salt very frequently while engaged in his experiments, felt a general excitation similar to that which is uniformly produced by coffee. Bailly,† who administered to himself one hundred grains in a few hours at Rome, states that "he carefully examined himself and *could not* perceive any symptom of *irritation*, which such a dose would certainly have produced if such had been its nature." Unfortunately, however, he did not record the effects produced in his case, and he only left us to infer its effect on himself from his statement that "it is a *sedative of the nervous system* and solely of certain periodical and intermittent functions of the same system, for it has no action on sensibility or locomotion." We would merely observe that it is a remarkable fact that such a quantity of the salt did not produce more sensible effects. Bailly, who in the year 1825 was assured of the stimulant action of quinine, was convinced afterwards that this action was *antiphlogistic* and *sedative*. Instead of producing thirst or irritation of the stomach, it cleansed the tongue, alleviated pain, *moderated the animal heat*, and *lessened* the *frequency* and *force* of the *pulse*. This last effect has been placed also among the most constant by Banquier, who observed as well as Bailly, that the *pulse* was *reduced* by *quinine* to *sixty-five* and even to *forty-five beats* per *minute*.

---

* Op. cit., 51.

† Traité Anatomico-Pathologique des Fièvres Intermittentes, etc., Paris, 1825, p. 424.

Professor Giacomini, in order to determine the effects of quinine, instituted a series of experiments on himself, which, from the high character, position, and learning of the author, deserve more than a passing notice, and which we therefore translate from his excellent treatise: "In the midst of these dissensions on the effects of quinine, I have thought that I could not do better to inform myself than by experimenting on myself, so I administered to myself at different periods in the winters of 1826 and 1829 repeated doses of the sulphate of quinine. I enjoyed at this time excellent health, although I was rather slender in person and very sensitive to the mildest excitants. My observations were made from nine o'clock in the afternoon until two or three o'clock at night, whilst in bed and occupied in preparing the materials of my lectures. I have noted exactly the doses taken, the various states of my system and the atmosphere, and my feelings in clear, rainy, or humid weather, before and after sleep; in the course of the experiments and afterwards. The variations in the pulse have been noted exactly, whilst sitting or lying down. I will not reproduce the journal of my notes, for it would be too long and tedious. I will limit myself solely to the indication of definite results. During the forty-six days of my first experiments, the pulse increased two or three beats per minute at five periods only. This happened in the first experiment, having taken only six grains of sulphate of quinine, and in two others when the wind came from the southeast, and I experienced malaise and thirst; and lastly, in a fourth experiment, after having drank *two ounces of rum.* There existed then particular circumstances to which this increased frequency of the pulse might be attributed, for at the other periods the *pulse constantly fell* from four to six beats per minute, and often even to twelve, especially when I took sixty grains in the course of the night. The greatest diminution occurred when I retired to bed, or at the moment of awaking from sleep in the morning. When the doses were less than fifteen grains, my head was less affected and I felt more lively, although feeling a certain sense of general disquietude. The large doses made me *somnolent, disturbed* my *ideas,* and were attended with *ringing* in the *ears* and *deafness.* When in the course of the night and until ten o'clock the following morning I had taken in small quantities at intervals sixty-eight grains of sulphate of quinine, my pulse, which before the experiment gave sixty-four beats, was only reduced eight or nine pulsations, but it became feeble. I had fallen asleep sooner than usual and perspired very freely throughout the whole night, although it was winter. On awaking I was feeble, depressed, and my head felt heavy. On arising from bed, I experienced vertigo and walked with difficulty. This state of depression and suffering continued until dinner-time, when the deafness and general malaise ceased. Usually my appetite was increased, my mouth was clammy, but was never so after having eaten; the urine was more or less copious. I could not perceive any change in the intestinal evacuations. The first effects of the pulse manifested themselves an half-hour after the administration of the salt. Twice I combined the sulphate of quinine with two ounces of rum. The first time I took it with the rum, when ten grains of it were used, deafness and frequency of the pulse were observed. The second time, having drank the rum before, and which increased the pulse eight beats in a half-hour afterwards, I took fifteen grains of the sulphate of quinine in two doses an hour apart. After having slept, it had declined seven pulsations, and in the morning it was reduced twelve pulsations below its habitual standard. I did not experience any uneasiness in the kidneys or bladder, nor any heat in the stomach, except once, when I was a little more thirsty than usual, and which arose from other causes. A slight injection of the conjunctiva occurred from the use of the rum alone, which was dissipated by the insufflation of the sulphate of quinine on the affected organ, which removed the phlogosis as by enchantment, without producing any heat, smarting, or flow of tears. If, therefore, I must declare my opinion in regard to the dynamic action of the sulphate of quinine, I am enabled to say that it is exactly the reverse of that of alcoholic liquors,—that is to say, *hypothenisante*, as I have proved many times on myself. This opinion can only be contested by the production of as many or more experiments, equally exact, demonstrating the contrary; or at least by proving that the above experiments are inexact or inconclusive."*

M. Guersant is the next author in point of time accessible to us who has recorded his opinions on this part of the subject. As we desire to discuss the question impartially, however opposite the views expressed may be, and as his opinions are entitled to high respect, we quote them at length.†

"The sulphate of quinine produces very slight effects on the gastro-intestinal organs in their normal state. A sensation of warmth in the region of the stomach and slight pain has been observed in a few individuals. It rarely provokes vomiting, but it sometimes produces intestinal pains, especially when the canal is in a state of inflammation. The solution and absorption of the sulphate of quinine in the stomach is effected with great facility and promptness, owing to the acids which it contains. From the intestines it passes rapidly through the urinary passages, and at the end of two hours from its ingestion it is found in the urine. The influence of the sulphate of quinine on the circulation is not appreciable in all persons; however, it sometimes produces a remarkable reduction of the natural rhythm of the pulse. This phenomenon, which was remarked by M. Bailly, has been verified by several French and foreign physicians; nevertheless, it is far from being constant. M. Piorry, who has very frequently given the sulphate of quinine in large doses, states to me that he has never observed it. As to myself, I have observed it such a great number of times in healthy persons and patients, that I cannot doubt its reality. I have seen the pulse diminish from eight to ten pulsations in a half-hour, altogether from the administration of quinine in doses from fifteen to thirty grains. But when I have observed this effect on myself, I have found that it coincided with some slight precordial anxiety, so that it is probable that this action of the sulphate of quinine on the circulation is only the secondary result of its impression on the ganglionic nervous system. Whatever, though, may be the cause of this physiological effect, the principal phenomena first produced by the sulphate of quinine are displayed on the nervous system. Almost immediately after its ingestion into the stomach it produces a kind of heaviness of the head, or transient *deafness*, *vertigo*, *dazzling and disturbance of vision*,—sometimes a species of hallucination, and sometimes even a kind of temporary intoxication, analogous to that produced by champagne wine. This singular effect surprises and annoys the patient or persons affected when they have not been forewarned. More often, however, the sulphate of quinine only produces a few of the physiological phenomena we have mentioned,—*deafness* alone being *constant.* When the physiological effects produced by the sulphate of quinine arrive at such a degree as to affect the *senses* and to disturb the *mind*, then these nervous disorders are followed by *depression*, *debility*, and *difficult locomotion*, but these primary effects are not usually of long duration, unless the salt is continued in large doses and at brief intervals. In the majority of ordinary cases, one or two hours after the reception of quinine into the stomach, a slight reaction supervenes; but it is almost always appreciable. This species of perturbation produced by the sulphate is soon replaced by a state of *calm* and *comfort.* The pulse resumes its normal rhythm when it has been lessened; it becomes stronger and more full; a gentle warmth extends over the whole body, and is often accompanied with more or less perspiration, especially when the sulphate of quinine is given in divided doses; lastly, a feeling of strength succeeds to that of depression and debility. These phenomena do not always present themselves in this regular manner, and the action of sulphate of quinine, like that of all powerful medicines, sometimes presents great anomalies, according to the different idiosyncrasies of persons in health and disease. Certain individuals cannot endure this medicinal agent; it produces in them, even in small doses, taken by the mouth or enema or by frictions on the skin, sensations of heat in the stomach, colicky pains, or diarrhœa. In others, an inexplicable distress, great anxiety accompanied with chills, prostration, cold sweats, agitation, and even in some acute pains in the limbs, trembling, and cramp occur. In a small number of cases, the sulphate of quinine, without causing all the symptoms, excites a veritable febrile movement, more or less continuous, even when the digestive organs are in the best possible condition. On the other hand, persons in health and in disease have been observed who could support enormous doses of sulphate of quinine without experiencing any sensible effects themselves, or which could be perceived by others. M. Piorry has assured me that he has often given sixty, seventy-five, and ninety grains of sulphate of quinine in the space of a few hours, and has never observed any notable change except a temporary *deafness.* In some cases this physiological phenomenon has been carried to an extreme degree, and the *deafness* has become *permanent.* M. Itard had already cited this fact, and remarked that several deaf-mutes owed their infirmity to the administration of the sulphate of quinine. M. Meniere has also assured me that he has seen several cases of deafness in persons who had taken large doses of quinine for the cure of intermittent fevers. However, it appears probable that those persons who have become deaf after the administration of quinine were already predisposed to that sad infirmity, and that the salt of quinine has only acted as an *occasional* cause."

---

* Traité de Matière Médicale, 339.

† Dictionnaire de Médecine, tome xxvi. pp. 565–70.

The principal physiological effects of large doses of sulphate of quinine, even when they have not been given to such an extent as to produce poisonous effects, have been none the less sedative and perturbating to the nervous system; but must we conclude with M. Giacomini, because the sulphate of quinine acts, more or less, at first on the general system as a depressing agent, that this salt is a veritable *hypothenisante*, whose effects are analogous to blood-letting? This method of reasoning is evidently paradoxical. We must properly distinguish the two very distinct periods of its action in this regard, viz., a primary state of action, and reaction. In the first period, the sulphate of quinine, in large doses, truly appears to act particularly on the ganglionic and cerebrospinal nervous systems, and particularly on the organs of relation, which it temporarily enfeebles; but if the large doses of the sulphate of quinine are not frequently repeated, or if they have not been sufficiently potent to affect the cerebro-spinal system profoundly, then the reaction takes place more or less promptly, the vital powers are reanimated, and a new exciting influence of the innervation extends itself throughout the whole economy. The same occurs, besides, with other medicinal agents which are evidently stimulants, as alcohol for example. Moderate doses of alcohol increase the activity of the cerebro-spinal system, whilst excessive doses, on the contrary, often precipitate the healthy man into a state of prostration and intoxication, which has some resemblance to the action of quinine in large doses. In truth, do we not observe in syncopal intoxication paleness of the face, coldness of the extremities, failure of the pulse and strength, inability to move, and stupor of the senses; and are not these physiological phenomena the same as those in cases of poisoning by the sulphate of quinine, so that we might call it with reason the *intoxication of the sulphate of quinine?* We do not pretend to establish a perfect parity between the physiological phenomena produced by alcohol and those produced by the sulphate of quinine; the analogy is doubtless not perfect. Each medicament has its peculiar mode of acting, and we do not seek to explain that of the sulphate of quinine by comparing one with the other. We wish only to show that the sulphate of quinine, under certain circumstances, like alcohol, may present physiological phenomena of action and reaction, and may appear successively *hypothenisante* and *hyperthenisante*, according to the dose administered and the period at which the effects which it produces are observed.

M. Guersant concludes his observations, in regard to the physiological action of quinine, by declaring that its primary effect is to diminish the frequency of the pulse, to lessen the sensibility of the organs of hearing and sight, and to enfeeble the organs of locomotion; and reacting afterwards on the general system to increase all the functions, and particularly those of secretion and perspiration. These views are certainly peculiar in some respects, as will hereafter be discussed.

As far as our investigations have extended in the works accessible to us we find but few observations recorded of experiments having been made on man in health in *our own country*. These are slender materials, though interesting. Dr. John Harrison, then Professor of Physiology and Pathology in the Medical College of Louisiana, in an essay on Yellow Fever,* written in 1845, gave brief notes of four cases, which we quote literally.

"Before venturing to give the sulphate of quinine in such large doses, and upon such a raging fever, Drs. Hunt and Mackie performed a number of experiments to test its physiological action. The experiments were performed in 1839, at the Charity Hospital, upon *convalescents* from *different* diseases. From notes furnished me by Dr. Hunt I transcribe the following cases:

---

* New Orleans Medical and Surgical Journal, ii. 331.

"CASE 1.—At twenty minutes of 10 A.M., pulse 72; took fifteen grains sulphate of quinine. At 11 A.M., pulse 60; has *slept;* complains of heat at epigastrium; feels a little dizzy; pupils dilated. At half-past 12 P.M., no other change.

"CASE 2.—At 10 A.M., pulse 56; took eleven grains. At 11 A.M., pulse 48; has *slept;* has slight ringing in the ears; sweating freely a short time after taking the quinine. No restlessness

"CASE 3.—At fifteen minutes of 10 A.M., pulse 64; took nine grains. At 11 A.M., pulse 52; has *slept;* pupils slightly dilated; no other change.

"CASE 4.—At fifteen minutes of 10 A.M., pulse 100; took twenty grains. At 11 A.M., pulse 96; has *slept;* pupils slightly dilated; no other change. At fifteen minutes past 11 A.M., took fifteen grains. At half-past 12 P.M., pulse 92.

"All these cases were watched. The effects are as narrated. They gradually wore off without any other change.

"It may be mentioned here, that when the sulphate of quinine was given in large doses, a part of it was found, in the experiments made for that purpose, unaltered in the urine."

The views of Dr. Wood, late Professor of Practice of Medicine in the University of Pennsylvania, have been prominently placed before the profession for many years. They, however, deserve especial mention here, not only on account of the distinguished source from which they proceeded, but for the reason that they may be considered as representing the views of a large portion of the profession in this country. In his "Treatise on Therapeutics and Pharmacology,"* after describing the effects of sulphate of quinine as a tonic at length, and which are so familiar as to need no repetition, he states: "Admitting quinia to be moderately stimulant in small doses to those cerebral functions which it specially affects, we have next to consider the question, whether the sedative effects undoubtedly produced by it, when largely given, are direct or indirect; that is, whether they proceed from an immediately depressing influence excited by quinine upon the encephalic centres, or are the consequences of a preceding state of excitation. To solve this question, it must first be determined what are the immediate effects of a large dose of the medicine sufficient to induce the ultimate prostration. Close observation upon the human subject and the lower animals has shown, I think, that so far as the brain is concerned, these effects are such as characterize excitation. The flushed face, the feeling of tension or fulness in the head, the sensitiveness to light, the buzzing and roaring in the ears, the vertiginous sensations, the involuntary muscular movements, the increased frequency of pulse and heat of skin, and the active delirium and convulsions which occasionally, though rarely, occur, are all proofs of stimulation and active congestion of the brain; and these proofs are still further strengthened by the fulness of the vessels of the pia-mater, universally observed on post-mortem examination, and the evidences of positive meningitis, which have been observed in a few instances. It is true that these phenomena of excitation are much less observable when the same quantity is administered in small portions, at intervals of an hour or two; but in this case the stimulation from the several portions, not exceeding the degree of tonic action, is scarcely observable in the pulse, and subsides before being fully reinforced by the succeeding doses; while the secondary depression of the whole accumulates, and in the end becomes very obvious. The excitant effects of the large, single dose may continue for two or three hours, when they gradually subside into a contrary condition, proportionate to the quantity taken; and when this is in great excess, the prostration is in the end extreme.

---

* Vol. i. pp. 242–44.

"*Now, this is the ordinary and necessary result of over-stimulation; and it is altogether supererogatory to imagine the existence of a directly depressing power* in the medicine. The *stimulation* of an organ *first* excites its function; if it be continued and increased, the function is disturbed, and becomes irregular; if still further increased, the organ is *overwhelmed by the congestion induced*, and its function is impaired or suppressed. The first excitement is thus followed by depression; and this is deepened through another physiological law, which determines that the excitability of a part is exhausted by over-exercise. Thus, after the first excitant effects of quinia, above referred to, have continued a short time, the cerebral centres become incapacitated for their duties through *their congestion and secondary exhaustion*, and cease to send forth the influence necessary for the support of the functions over which they preside or which they in any degree control. Hence the diminution or loss of hearing, the occasional loss of sight, the general feebleness of the muscular power, the trembling, the gradually diminishing frequency and force of the pulse, the coldness and pallor of the surface, and the universal prostration. Now, this is a very different condition produced by a direct sedative to the nervous centres, or to the heart itself; and though it might prove useful in certain cases if safely induced, yet in determining upon the propriety of having recourse to it, reference must always be had to the possible danger of the great over-excitement and congestion of the nervous centres involved."

It will be seen that the facts and opinions of the authorities cited not only in regard to the phenomena observed, which followed the administration of quinine, but in respect to the *modus operandi* of the salt, are entirely opposed to each other, and are in many respects altogether irreconcilable; and were we to stop here, we would approach the treatment of the diseases in which the agent is usually employed, assailed by fearful doubts and anxieties; yet we shall see hereafter that the dispute is rather physiological than practical, and that when these contestants meet at the bedside, they are often singularly unanimous in their therapeutic procedures. Let us proceed there with them. Let us carefully examine the symptoms and nature of the disease which they all succeed in removing or mitigating; and then having carefully observed the effects of the remedy in disease, recur to its physiological phenomena. By comparing one with another, we trust that we may arrive at or approximate a satisfactory solution of the question.

EFFECTS IN DISEASE.

As it was in the treatment of diseases of the intermittent class that the parent tree of our valuable remedy was first introduced, so we find the first experiments with the new remedy were made in those maladies; yet we find such diversity of doctrine in regard to the nature of that species termed fevers, that we prefer to investigate its action first in the simplest form of intermittent disease, viz., *in neuralgia.*

It is well known, and admitted, we believe, by all practically conversant with the subject, that neuralgia of a strictly periodical character is often produced by the same morbid agency which gives rise to simple intermittent fever. Prevailing in the same localities, prevalent in the same seasons, preceding alternately with, and succeeding to, periodical fevers, exhibiting the same types, the same phenomena of intermission and remission, and yielding to the same treatment, the identity is almost perfect, except the frequent absence of fever, which is, however, present sufficiently often to make the similitude complete. These neuralgiæ are the *febres topicæ* of the old writers, the *fièvres larvées* or *masquées* of the French, mentioned by Morton, Van Sweiten, Huxham, Senac, Casimir Medicus, Sauvages, Chomel, Mongellaz, Bonnet, Nepple, Macculloch, Holland, Drake, Jolly, and others, to whose works we refer the reader who has any misgivings on the subject. These neuralgiæ may be seated in any portion of the cerebro-spinal or ganglionic centres, or in the minutest branches alone of the nerves of either of those systems.

Of this affection, let us take up *toothache*, not only on account of its apparent simplicity, but because here the disease is almost present to our vision; we can almost see here the morbid process. Let us illustrate it by a case.

We were called to see a gentleman afflicted with this painful malady. He experienced the most intolerable agony, which he thought arose from a carious first molar of the lower jaw; but said that all the teeth of that jaw on that side seemed painful. As the suspected tooth had a very large cavity, and was entirely useless, I extracted it and left him apparently relieved. Again I was summoned to attend him on the evening of the next day, and found his condition much worse. The tissues of the whole face on that side were very much swollen and of febrile heat, the pain in the jaw, which he now referred to the molar tooth next to the seat of the one extracted, was extremely violent, amounting to agony. The muscles of the jaw were swollen, tender, and rigid to such a degree that it was impossible to open the jaws more than half an inch. He had taken a large quantity of laudanum and a quart of brandy (though a temperate man), but with very little relief.

He informed me that on the morning before, after extracting the tooth, the pain was almost relieved, but that it returned in the evening, and on the next morning (that of my second visit) the pain remitted again, but soon returned, and placed him in the condition I found him. Suspecting the malarial origin of the affection, I gave him twenty grains of quinine at a dose. In half an hour he was asleep, for the first time in thirty-six hours. His pulse, which had been excited, became tranquil; the skin, which had been above the normal temperature, and dry, became soft, moist, and of natural warmth, and next morning, on awaking, the pain had vanished, and the inflammation of the muscles of the jaw and general swelling of the face had diminished to such a degree that he could eat his breakfast, and after continuing the medicine for two days in ten-grain doses, he was entirely recovered.

Now, what was the nature of this affection? He lived in a malarious district, and had been subject to intermittent fever; he had been first attacked with pain in the dental nerve of a remittent character; whether that pain arises from inflammation of the nerve or not is a mooted question; let us therefore call it irritation; this irritation continuing gives rise to all the phenomena of inflammation in the surrounding tissues. The sulphate of quinine relieved this pain; it subdued the inflammation; it produced sleep; it reduced the pulse; and arrested the fever. Here plainly it acted as an *anodyne, narcotic, and sedative.* Its effects were not analogous to alcohol, for that failed. It was more potent than opium, for that remedy had been taken in an otherwise dangerous quantity, and failed to relieve the pain but slightly, and was utterly impotent to induce sleep.

To demonstrate more clearly the nature of this affection and the effect of the remedy, we quote interesting cases from other writers:

"In the month of February, 1820, a child aged four years was attacked for the first time with intermittent fever, during which he complained violently of a pain in the teeth. A second paroxysm returned the third day, and was characterized by the following symptoms: teeth dark, but clean, as if they had been plugged with lead; tongue red; extreme thirst; respiration laborious and frequent; pulse strong and hard; odontalgia general, evoking the cries of the child, although his teeth appeared sound.

"M. le Docteur Goury, recognizing a tertian fever, of which the predominant symptom was odontalgia, rejected the application of leeches to the epigastrium, which had been advised, and prescribed a potion composed of a drachm of extract of cinchona, a quarter of a grain of extract of opium, and an ounce of syrup of cinchona in four ounces of distilled water of centaury, to be taken in divided doses. He prescribed as a drink an infusion of chamomile mixed with good wine. The day following, the teeth appeared very white and healthy; the child was very lively, and felt no effects of the access of the preceding night, which having commenced at seven o'clock in the morning, terminated like the first, at two o'clock in the afternoon. To this day of intermission a third access succeeded, which was very short and less violent than the preceding, and during which the odontalgia was supportable. The same prescription was ordered, only it was increased by the addition of a half-drachm of extract of cinchona to the potion. The fourth access was still less intense, and the fifth entirely failed to appear. The same treatment was continued for four days to insure the cure; this appeared to be secured, when three weeks after the child experienced another attack of fever and odontalgia; but this time, in place of the quotidian, it assumed the quartan type. The same treatment so moderated the second paroxysm of this *novel fever*, that the third did not take place. Since that period, the little boy has enjoyed excellent health."*

The reader will perceive that in this case the symptoms of intermittent fever were so completely intermingled with those of neuralgia that they cannot be separated; they had the same march, the same relapses, and the same change of type; they were evidently one and the same disease, and yielded to one treatment. The following was an analogous case:

"A delicate young lady of a nervo-sanguine temperament, residing at a woollen manufactory, was affected for eight days with a simple quotidian fever (September, 1823). A few grains of opium arrested the disease. But three days afterwards the patient was awakened suddenly by a violent acute pain in the last superior molar tooth, which was carious. The pain extended over the whole of the lower jaw, the upper part of the pharynx, and the muscles of the tongue, producing in these parts a horrible, painful, tetanic contraction. All these symptoms of suffering disappeared suddenly in the morning, to reappear in the same manner at the same hour every night. The fourth day I extracted the tooth, and in place of the odontalgic paroxysm the primitive intermittent fever again appeared. This passage of an intermittent fever to a neuralgia, and of the latter to an intermittent fever of the same type, prove that these two affections do not differ in their nature, and are related to the varying phenomena exhibited by the nervous system."*

---

* Goury, Bulletin de la Faculté de Méd., No. 8, quoted by Mongellaz, "Des Irritations Intermittentes," i. 222.

The following case not only displays the properties of the sulphate of quinine, but tends to throw some light on the pathology of malarial diseases:

In the summer of 1866 I was called at night to see an infant male child only six months old, exhibiting the usual symptoms of infantile colic. The usual remedies only had a momentary effect in allaying the violent paroxysms of pain. In the forenoon of the next day, however, the child seemed relieved, but I was summoned on that night to attend him again with the same symptoms, which continued until noon, when remission of the symptoms recurred. About three o'clock at night, as before, the symptoms recurred with extreme intensity, and, in addition, evidences of unmistakable inflammatory action set in. The child had fever, the abdomen was hot, tumid, and exquisitely tender on pressure. The treatment hitherto pursued consisted in the use of aperients, anodynes, and antispasmodics, but the symptoms now assuming a grave character, and the periodical character of the disease being evident, I determined on the employment of the sulphate of quinine. Three grains were given in three doses, at intervals of four hours, but the paroxysm recurred at night. Five doses of one grain each were now administered throughout the day. Under the operation of the quinine the child fell asleep, and continued in deep slumber for twelve hours. The fever declined; perspiration ensued, the pulse fell from 160 to 100 beats per minute, and the paroxysm was averted. Rapid convalescence ensued under the use of the same remedy in diminished doses.

---

* Essai sur les Fièvres Rémittentes et Intermittentes, par T Frédéric Nepple, D.M.P., Paris, 1828, p. 232.

Here evidently the ganglionic nerves were the seat of neuralgia, which developed inflammation of the intestines,—both yielding to the same treatment and resisting every other means.

Let us now pass on to the interesting subject of

Periodical Fever and observe the effects of the sulphate of quinine in the various forms and grades of disease classed under that title. The virtues of the sulphate of quinine in simple intermittent fever are too well known and admitted to require discussion. All writers admit its potency in this form of the malady, however they may differ in the method of its employment; but its use in the remittent and pernicious forms has been the subject of much controversy. On the other hand, there are some who contend that its exhibition should be restricted to the stage of remission, and that it is hazardous to employ it while active fever is present; whilst, on the other hand, many as strenuously insist upon its speedy administration without reference to the degree of fever, and in despite of the presence of symptoms denoting inflammation of the vital organs.

Cases of mild character, we well know, will recover without the exhibition of quinine or any other remedy; the disease being often self-limited in its character and terminating in health either from the elimination of its cause or the exhaustion of susceptibility to its action, or, as some regard it, from the curative powers of nature. But it is needless to state that many cases of remittent and even simple intermittent fever which appear at the onset to be devoid of danger, frequently assumes a dangerous and menacing character, and that it is therefore impossible to predict at the commencement of an attack what its subsequent course and gravity may be. "To wait for a remission," as the phrase is, will often be equivalent to the loss of a patient, and has been justly termed a "meditation on death." Nor is the remission the most favorable period for the administration of quinine. If we examine the course of the disease, we will find that in the large majority of cases the exacerbations are ushered in by a condition resembling a cold stage, however imperfectly developed it may be, and often eluding vigilant observers. In many cases this imperfect cold stage is only marked by a *slight coldness* of the *extreme parts*, such as the *tip* of the *nose*, *toes*, and *fingers*,—the *rest of the body maintaining a febrile heat.* This diminished temperature is often unperceived by the patient, who, on the contrary, has only febrile sensations during its existence; but however slightly marked the cold stage may be, or even if it be entirely imperceptible, we know from the very nature of the disease that there is a period in its course which corresponds to the cold stage. Now, the *remission* almost always occurs *just before* the period of the cold stage; and if quinine be given in the remission, which, in the large majority of cases, is a very *brief* period, its *full effects* will not be obtained in time to prevent the cold stage or the succeeding exacerbation. Given, then, in the remission, it has to incur all the difficulties in the way of absorption to which all medicines are liable in an *ascending fever*, and in the presence of *high exacerbation.*

At what period, then, is it most advantageous to administer the remedy? If we examine the natural history of the disease we will surely ascertain that the exacerbation, in the vast majority of cases, takes place in the afternoon or at some period of the evening before midnight; and that the cold stage very rarely occurs between nine o'clock P.M. and the rising of the sun of the following day. Close observation for forty years in regions rife with malarial fever has convinced us of this fact; and also that, however high the fever may be, or however continuous in its character, the febrile action commences its natural decline at some period of the latter hours of night. This is the period we then select for the administration of the sulphate of quinine. It will be sufficiently early to anticipate the next paroxysm, and to prevent this is all that is necessary for the safety of the patient. We know well from our own observation that the remedy may be given at the acme of the exacerbation without dangerous consequences, but it is an *unfavorable period* for its *administration.* The *stomach* then is in its *most irritable condition,* often rejecting the *blandest fluids.* It is a period in which the *absorption* of the salt takes place with *most difficulty,* and in which its unpleasant effects on the brain, embraced in the term *cinchonism,* are most *readily developed.* Given at night, however, when, as we observed, *more* or *less* declension of the fever usually occurs, it tends to hasten the *downward tendency* of the fever. Its *power, in full doses,* to produce *repose and tranquillity of the cerebro-spinal system* is ASSISTED by the *natural* and *habitual tendency* of that *division* of the *nervous system* to *repose* in the *night season.* It reduces the febrile heat and the frequency and force of the pulse at *that period* with more *ease* and *certainty;* for it has *less arterial force* then to *overcome;* and when the usual period for *remission* arrives, the patient is completely under the influence of the agent and fully prepared to resist the onset of the next paroxysm. *Whether,* however, *there is any* *sensible decline of fever* or *not*, the coming *day* ought not to *dawn* upon a patient *unprotected* against the perils of the *surely approaching paroxysm. That is a certain danger*, which no one will contest. The *hazard* of the effects of quinine *admits* of *question* when given in *reasonable* quantities and otherwise *judiciously* administered; or if this be denied, the *danger of another exacerbation* cannot be. At the worst, then, we oppose a means of *doubtful* hazard against a *certain* calamity. The surgeon who would refuse to use his knife in a case where the chances were in favor of his patient from the exercise of his skill, would be guilty of no greater dereliction than the physician who would expose his patient to the pitiless mercy of disease because half of the world told him that there might be some danger in the means, and the other and better half told him there was none. In making these declarations we intend no disparagement to those who entertain different views, but we shall prove hereafter that *these views are not held* by those who have had the *best* and *most frequent opportunities* of *combating* the disease under consideration, and that *they must yield* to the unanswerable logic of indisputable *facts*.

Let us then inquire what are the effects of the sulphate of quinine in the disease under consideration, when taken in the midst of febrile action, as reported by those who have had the best opportunities of forming a correct conclusion. In ordinary affairs, when a matter is in dispute, we summon our witnesses and interrogate them, and when two parties of equal intelligence and veracity give contrary opinions, we decide between them by an inquiry into their relative opportunities for observing, and the number of corroborative or demonstrative facts they present. This is the common-sense and common-law rule which we shall endeavor to apply in the decision of the question before us. To demonstrate the effects of the sulphate of quinine in remittent fever, we must first glance at the leading features of that disease, and then by observing the changes which occur after the administration, we shall be able to form some idea of its action.

The *onset* of remittent fever is generally sudden; and in cases where premonitory symptoms are present, they are usually of brief duration. The patient has an irrepressible foreboding of evil, is languid, inclined to be drowsy, and disinclined to exertion. He experiences fugitive pains in his head, neck, loins, and limbs, and sensations of chilliness are felt running along the spine, and from thence irradiating to the extremities, succeeded by flushes of heat. The appetite fails, or is capricious; the tongue is slightly covered with a white fur; the bowels are generally costive, and occasionally alternating with diarrhœa; the urine is copious and limpid, and there is frequent micturition attended with a sensation of heat in the urethra.

The *invasion* is almost invariably ushered in by a chill, the sensation of cold varying from an evanescent tremor to a distinct and prolonged rigor, *which may occur at any time of the day or night.* This *initial* chill is usually felt sensibly by the patient, however, and the reduced temperature of the extremities is evident to the touch of the attendant. The patient is restless, sometimes amounting to extreme jactitation. He is thirsty, and complains of a sensation of internal heat; his breathing is accelerated in some cases, unequal, and interrupted by sighing and yawning; the pulse is frequent, small, and sometimes irregular; pain in some region of the head is usually present, as well as in the *spine,*—the latter often very acute and distressing, and constituting the principal suffering of the patient. Nausea and vomiting are occasional symptoms; but, according to my observation, not so generally present as it is usually stated. This stage, in ordinary cases, is commonly of short duration, and is soon followed by decided reaction.

During the *exacerbation* the skin becomes hot and dry, the face flushed, and a roseate glow is perceptible over the general surface. The eyes are injected, prominent, and unusually bright. The cerebro-spinal pains increase in intensity, and assume a throbbing character. The pulse acquires volume, force, and regularity, but is almost invariably *compressible*. The respiration becomes slower, more regular, and less laborious. The tongue becomes dryer and more coated, and the secretions of the mouth viscid and tenacious; the thirst continuing, but not usually so urgent as in the chill. These symptoms increase in intensity until they amount to an acme of exquisite suffering, and then gradually decline.

The *remission*.—Late in the afternoon, usually between the hours of five and eight, in very mild cases, but postponed to some period between midnight and sunrise in more violent attacks, the fever and its concomitants sensibly begin to yield, and the patient sinks, exhausted with suffering, into a slumber of variable duration, from which he awakes more or less relieved. The skin becomes less hot and relaxed, the tongue moist; the painful sensations abate, and often entirely vanish; the respiration becomes easy and free, and the pulse diminished in frequency and strength. This respite from suffering is usually, however, of short duration, being soon followed by the recurrence of the stage of congestion or chill. As the *succeeding chills*, however, differ in some important features from the initial chill, we devote to them an especial notice.

The *chill proper of remittent fever.*—This, according to my observation, never occurs between the hours of nine P.M. and the rising of the sun of the following day, but usually between the hours of eight A.M. and twelve M., and occasionally between six and eight P.M. At or near these periods the watchful attendant will perceive a sensible diminution of temperature of the extreme parts, viz., the nose, toes, and fingers,—or the whole hands and feet will be found below the natural standard, being cool and damp,—the *rest of the surface retaining its febrile heat,* more evident in the cerebro-spinal and epigastric regions. In this condition, the patient rarely complains of any sensation of cold, but often of heat, desires to be fanned, the clothing to be removed, and entreats for cold drinks. The pulse is frequent, but usually regular; the bowels torpid, but easily excited into action. Nausea and vomiting are sometimes present, the fluids ejected being usually of a bilious character. The respiration is not much affected, but the patient yawns, and gapes, and sighs deeply. The duration of this stage is usually brief, rarely lasting more than an hour, and is succeeded by the reaction, which is marked by an extension of the febrile heat over the whole surface, and a repetition of the symptoms of the first exacerbation just described. As the disease advances, the pulse becomes increased in frequency, quickness, and tension, but diminished in volume. Evidences of organic irritation or inflammation of some one or more organs become developed. The tongue becomes more coated and acuminated, with a perceptible redness at its extremity and on its borders. More or less tenderness on abdominal pressure will now be felt, with gastric and intestinal irritability, attended in some instances with an intolerable burning pain, most intensely felt during the chill. Percussion will generally detect an increase in the size of the spleen, and later, the hypertrophy becomes evident to the eye, particularly when the patient is in a sitting posture. Diarrhœa may now make its appearance, but usually is postponed to an advanced period; but it now may be observed that aperients of the mildest kind are prone to produce intestinal spasm and hypercatharsis, and particularly near the chill period. The disease now progresses with aggravation of the cerebral and gastro-enteric symptoms until, from the third to the fifteenth day, it usually terminates, without the interference of art, in fever of pernicious or algid character, or of a more continued type, or in intermittent fever.

Such are the symptoms observed in the course of an ordinary attack of remittent fever, the conspicuous features of which are cephalalgia, restlessness, quickened respiration, excitement of the heart and arteries, nausea and vomiting, and all this with great disturbance and exaltation of the calorifacient function. In the more severe grades all of these symptoms are aggravated, and delirium, convulsions, and coma betoken the serious involvement of the brain and spinal marrow; uncontrollable nausea, bilious vomiting, gastric pain, and abdominal tenderness pronounce the stomach, liver, and bowels to be seriously implicated, whilst the prominent enlarged spleen tells of its distention and congestion.

When we examine the cadaver, what an array of lesions present themselves! No part of the system seems to escape injury. Inflammation of the brain, spinal marrow, and the gastro-enteric mucous membrane, various alterations of the liver in consistence, color, and size appear; nor do the lungs escape, pneumonia of the most fatal character having often been observed arising as a consequence, a legitimate lesion,* or accidental complication.† Now, the sulphate of quinine has been given thousands of times in all the varieties, types, and grades of remittent fever in Europe, Africa, Asia, and America; it has been given in all of the stages of the disease and in every variety of dose, and with the most beneficial results. If human testimony avails anything, then we have the most overwhelming proofs of its efficacy from those who have had unlimited opportunities for observing the malady in its most perfect development. Its action has been carefully watched from the moment of its administration to the hour of recovery; cases, the records of which would fill many large volumes, have been given to the world in illustration, and it would seem that if the rules which should guide its *therapeutic use* and the mode of preventing its abuse could not be laid down now we might almost despair of their ever being accomplished.

---

* "J'avais établi, contrairement à l'opinion commune, que la pneumonie, au lieu de suivre une marche continue, pouvait se montrer avec un des types des fièvres palustres, reconnaître pour cause la même infection miasmatique, et céder promptement à la même médication spécifique." Grisolle, Traite de la Pneumonie, 2me édition, 411.

† La Roche, "Pneumonia and Malaria," pp. 502.

To the French physicians we are indebted for the first experiments with the sulphate of quinine in remittent fever. We have the authority of M. Magendie for the fact. He states that "M. Renauldin communicated the first case of this nature," and that shortly after he, "M. Magendie himself, had an opportunity of administering the same medicine with success."* This was published in his *Journal de Physiol.*, July, 1821. In 1822, Drs. Rossi, Tonelli, and Matthias also employed the sulphate of quinine in remittent fever with success. The statement was published in the *Giornale Arcadico di Scienze* at Rome, November,

---

* Magendie's Formulary, ed cit., p. 52.

1822, xlvii. p. 129, which was noticed in the *Journal of Foreign Medical Science and Literature*, vol. iv. 347, published then at Philadelphia in 1824. We are not informed concerning the special effects produced by the remedy in these journals, but the reviewer states "that it has a rapidity of effect, especially in *pernicious* and *sub-continued* intermittents, far surpassing that of the bark, and that it was proven that large doses produce no bad consequences; in other words, that it can never act poisonously; that it may be safely given to persons of all ages and temperaments, to pregnant, puerperal, and menstruating females; and that when it fails the failure is owing to accidental causes." "In 1823, Dr. Giacomazzi, of Brescia, declared that the sulphate of quinine was a very powerful *contra-stimulant*." *

In the *Medical Recorder*, of Philadelphia, vol. xi. 174, appeared an analysis of a paper written by Dr. H. Perrine, which appeared in the Philadelphia *Journal of the Medical and Physical Sciences* of November, 1826, entitled "Large Doses of Sulphate of Quinine in Fevers," in which is quoted a case of malignant remittent fever which was cured by large doses of the remedy, "eight grains being administered every third hour until sixty-four grains were taken." "Dr. Perrine closes his remarks by observing: My observations so far exhibit the following as one of the successful modes of treating our autumnal fevers, whether congestive or inflammatory: bleeding whenever the symptoms require it, a dose of from six to twelve grains of sulphate of quinine every two or three hours at any period of the *fever*, until its symptoms in the pulse and skin are subdued. Then purgatives to obtain copious, consistent evacuations from the bowels until they regain their usual power. Subsequent attempts to *form fever* should be counteracted by a large dose of the quinine."

---

* Giacomini, Traité de Matière Médicale, 349.

We have thus far traced the introduction of large doses of quinine as a sedative in fevers into this country, and we believe that *Dr. Perrine has the honor of first promulgating that fact in America.* In Italy, where malarial fevers are habitually endemic, this practice early found its warmest partisans. M. Giacomini * states in several places in his works that Prof. Tommassini has considered the action of the sulphate of quinine as contra-stimulant, "and that as to Rasori all the world knows that he regarded that substance for a long period as a contra-stimulant." "Silvy, a French physician, is convinced that, contrary to the opinion professed in his country, that sulphate of quinine was an antiphlogistic remedy; he had observed, in fact, in sixty-five patients, that on the morrow after the administration of quinine the pulse declined from six to twenty pulsations, and that it did not rise again, although the dose had been increased to thirty grains a day. He did not observe any sign of *gastric irritation*, dyspnœa, nor *irritation of the urinary organs;* these symptoms, on the contrary, *disappeared under the use of the medicine.* Bailly,* who practised in Rome among the intermittent, remittent, and pernicious fevers prevalent there, who was perfectly familiar with their symptoms, progress, and morbid anatomy, and who has left on record an invaluable transcript of cases, in which every description of complication is faithfully described under the names of *Fièvres comateuses*, *dèlirantes*, *convulsives*, *épigastralgiques*, *gastriques*, *hèpatiques*, *péritoniques*, *gastro-enteriques gastro-cèphaliques*, *arachnitiques*, *splénitiques*, *et*

---

* Op. cit., 349.

---

* Traité des Fièvres Intermittentes Simples et Perniciéuses, Paris, 1825.

pneumoniques; in which all the organs of the great splanchnic cavities were involved either singly or combined, as shown by the phenomena during life, and proven by the examinations of the cadaver, did not hesitate to give the sulphate of quinine boldly, regarding it as the *sheet-anchor of safety,* "*the specific sui generis,*" a sedative of the nervous system, "*en un mot, une des plus belles acquisitions que la médecine ait faites.*" "A single bleeding," he states, "a single purgative, and a single administration of the cinchona terminates at once the malady." "I act against all the elements of these diseases; I *diminish the activity* of the vascular injection; I derange the *movements which tend to establish it;* I favor the absorption of that which may prove vicious in some portions of an organ or system of organs; in fine, I stupefy the periodical function of the nervous system. For the cinchona *does not* appear to me to possess the *stimulant and tonic properties which have been accorded to it,* and it does not cure diseases by inflaming the stomach; it is not by derivation that it prevents the return of the paroxysms. The success which has been obtained from its use in sub-continued pernicious fevers, in which the paroxysms are *not separated by appreciable inter-*

vals, and in consequence of which there should be present as acute lesions of the stomach as are commonly observed in the most violent fevers; conclusively proves that it may *suppress the paroxysms*, even when administered at the *height of fever*."

If, leaving the classic shores of Italy, we visit Africa, we behold the skilful and intrepid Maillot bravely battling against the concentrated miasms of that deadly clime, here are presented to us the most fatal examples of the force of that poison, more noxious than the upas, and which, like the thunderbolt of heaven, often destroys its victim at a blow. But little time is allowed here for argument as to congestion of the pia mater or gastric irritation. We must act on the instant, or death claims its victim. Here we observe our heroic remedy displaying its mighty power. To the brain, congested as in apoplexy, it brings rapid relief; to the cerebro-spinal membranes, which Maillot invariably found inflamed after death, we offer the agent which has been accused of inflaming them. And with what results? Let one speak who "came and saw and conquered." *

---

* *Vide* "Lettres sur la Traitement de Fièvres Intermittentes de l'Algérie, et.," par F. C. Maillot, Lille, 1846, p. 6.

"It is to you, my dear Maillot, that we owe this success; it is to you, who demonstrated to us the nature of the gastro-cephalic intermittents of Bone; it is you who fixed our attention on the pernicious fever which surrounded us, and who indicated to us its treatment. Before your arrival here, in 1833, I was witness of that summer crisis, during which we lost 1100 patients, and when I saw with grief all our methods of treatment failed. We *recognized perfectly the gastro-entero-cephalitis*, but the *treatment* applicable to that disease *scarcely ever succeeded!* So it was with enthusiasm that we adopted your medication, and by your example the sulphate of quinine, in doses of twenty, thirty, and eighty grains, *superseded blood-letting* with immense advantage. It is then to you, my friend, that we are indebted for a correct knowledge of the disease of Bone. It is with pleasure, I repeat it, because it is my conviction, and I desire to pay you this debt. Placed in an independent position, and sheltered from all spirit of ridicule and jealous rivalry, I am happy to render to Cæsar that which belongs to Cæsar. My testimony cannot be suspected.

"HUTIN,

Chirurgien en chef à l'hôtel royal des Invalides."

If we turn to the admirable work * of M. Maillot, in which he has recorded many illustrative examples of the pernicious fever of Algiers, and examine the symptoms of the disease so fully and faithfully detailed, we cannot fail to deduce a satisfactory opinion in regard to the effects of the sulphate of quinine. Characterized by all the symptoms of ardent fever, an "atrocious headache," delirium, convulsions, coma, *subsultus tendinum*, a hard, full, and frequent pulse, dry, burning skin, inextinguishable thirst, dry tongue, nausea, and vomiting; these phenomena disappeared "as by enchantment" under the use of the sulphate of quinine in doses of from twenty to eighty grains. It is true that this medicine was often preceded or followed by blood-letting, general and local, as was eminently proper; but the latter was found utterly insufficient to control the disease, without the employment of the sulphate in the most liberal manner. What can be the action of a remedy which *arrests such a disease*,—that *relieves active delirium*, *profound coma*, *reduces* the *pulse* to its *normal standard*, *allays intense febrile heat*, and all the *distressing symptoms of violent pyrexia*, in the

---

* Traité des Fièvres Intermittentes, Paris, 1836.

most prompt manner? Can it be an excitant,—a stimulant? Would any sane man exhibit a stimulant in such a condition of the system? Would the bravest, the most reckless, *dare* to throw into an organism, *excited to frenzy already*, an agent having the remotest resemblance to an *excitant?* If we were to admit that the remedy produced sedation by first exhausting the excitability of the system, *who* would *venture* on such a *perilous* and *circuitous* route, in the face of so many dangers to secure it? *To ask these questions is to answer them.* The issue here can only be avoided by irrational and incredulous scepticism. But neither doubts nor denial will here avail; the decision of the question does not rest alone on the cases or results of the treatment of M. Maillot, as numerous and well-attested as they are, although, as he tells us, they were "*many thousands* in number," and are corroborated by the majority of the physicians of Algiers. We shall see that they are attested by "a cloud of witnesses" equally as competent and veracious. We have the valuable testimony of Dr. Samuel A. Cartwright,* formerly of Natchez,

---

* Author of a Prize Essay on Malignant Fever (*Med. Recorder*, ix. p. 3); of another on Cholera Infantum, which received t

Miss., one of the most skilful and discriminating practical physicians which this country has ever produced, and the value of whose contributions to medical science has been recognized in every portion of our country. In an address before the Medical Convention of the State of Mississippi in 1846, this physician said that "Dr. Perrine (as we have before stated), Dr. McPheeters, and Dr. Metcalf, our worthy president, nearly twenty years ago, introduced the practice of giving quinine in our paroxysmal fevers." In 1826, Dr. Perrine, in his own case, took during the febrile paroxysm eight grains of sulphate of quinine at a dose, which reduced the pulse. Soon afterwards, Dr. McPheeters adopted the plan of giving quinine during the febrile paroxysm. In 1827, Dr. McPheeters and I used the quinine very extensively in large doses,—six or eight grains in an epidemic fever characterized by a very frequent pulse, and great determination to the head. We gave it in the febrile paroxysm, and found it to be much more effectual than in the remission of that particular fever." *

---

prize from Medical and Chirurgical Faculty of Maryland (*Med. Recorder*, x. 153), and another on the "Diseases Resembling Syphilis" from Harvard University (*Med. Recorder*, x. 428.)

* New Orleans Medical Journal, i. 732.

The record of cases presented by Dr. Wm. M. Boling,* of Alabama, in his excellent paper on the Treatment of the Inflammatory Diseases of Malarious Districts, illustrates the sedative and antiphlogistic action of the sulphate of quinine in remittent fever, complicated with various local inflammations, in the clearest and most incontestable manner. This physician states: "In almost every case, whatever the nature of the disease, supposing the system at the time to be laboring under the influence of malaria, either as the principal curative agent or as an important adjuvant, the best effects may be anticipated from its administration. This I have observed under its use in the inflammatory affections of the chest, that an abatement in the physical signs almost invariably *follows* —very rarely precedes an abatement in the febrile excitement, and a diminution in the action of the heart and arteries. Indeed, under its controlling influence over the sanguiferous system, the action of the heart may sometimes be reduced from a state of high excitement almost to a natural standard long before any abatement takes place in the local inflammatory action as indicated by the physical signs." Cases are then detailed in which meningitis, convulsions, acute bronchitis, pneumonia, dysentery, etc., promptly yielded to the remedy, assisted or not by the lancet and other appropriate treatment. Dr. Boling concludes his article with the following remarks:

---

* American Journal of Medical Sciences, vol. iii. (new series), 1844, p. 87.

"The *peculiar* applicability of the quinine to the treatment of the inflammatory affections of malarial districts, is owing to the combination with its antiphlogistic properties of a power as an agent in controlling the periodicity of morbid action. As an antiphlogistic remedy in elevated and healthy localities, it will probably never supersede the lancet, antimonials, etc., though it may in many cases be brought to their aid; but in malarious regions ere long it will generally be looked upon as the *safest* and most manageable *contra-stimulant* we possess, and at the same time one sufficiently powerful, while other agents of the same class will only be used to fulfil some casual indication, or as adjuvants to this the principal remedy."

Surgeon Charles McCormick, U. S. Army, has contributed the results of his extensive experience on this subject in the most earnest and positive manner. His whole paper is well worthy of transcribing, but as it is generally accessible and occupies much space, we must be contented with the following extracts:

"I have used the sulphate of quinine in large doses, say from four grains to thirty grains and upwards, constantly for four years. I have nearly always used it simply diffused in cold water as a vehicle. The average dose I usually employ in intermittents is from ten to twenty grains at bedtime, and a similar quantity the following morning, or three or four hours previous to the period of the expected paroxysm. In remittent and continued fevers, from twenty to forty grains is the average dose in which I administer it, to be repeated every twelve to twenty-four hours, or oftener, if necessary, until the fever is arrested."

"I have given it in large doses, under all circumstances, in the prodromic, the cold, the hot and sweating stages of fever, and during the intermissions and remissions; in simple, uncomplicated fever, and in fevers complicated with various local inflammations of the head, chest, and abdomen, and have never witnessed any injurious or unpleasant symptoms *when given in large doses.*"

"Given in large doses boldly and freely during the high febrile excitement of idiopathic and arthritic fevers, it will be found to lessen the force of the pulse, diminish the heat and dryness of the skin, relieve restlessness, and throw out on the surface a general, warm, and free perspiration; in short, in a few hours, generally from one to three or four, it will cut short the paroxysms and arrest the further progress of the fever; generally acting sensibly on the skin, occasionally on the secretions from the bowels; producing free alvine evacuations; acting also on the kidneys and bladder by causing a free secretion and discharge of urine; sometimes without any other sensible effect, the fever is seen to subside under the influence of this potent drug. The quantity necessary to produce these effects may vary in different cases; generally a dose of thirty grains will be sufficient. Where venesection is required, let the sulphate be given immediately after.

"Stimulants possess the power of exciting, and sedatives that of diminishing, the animal energies. Tonics are classed as permanent stimuli. If, then, a remedy may not only be *safely*, but advantageously given to patients laboring under high fever, acute rheumatism, and fevers with *various* local inflammations, it surely must be admitted that it does not possess the power of exciting the animal energies, and is not therefore a stimulant or tonic; for, as previously stated, such remedies are altogether inadmissible where the powers of life are in an exalted condition. And as on the other hand it is found to lessen the force of the pulse, heat and dryness of the skin, allay restlessness, and to throw out on the surface a general, warm, and free perspiration, if given at a time when the powers of life are in an exalted condition, its action more closely resembles that ascribed to the class of *antiphlogistics*. But it possesses other powers than those of antiphlogistic, and to these its apparent action as such is to be attributed. When given in large doses, I have seen it allay *pain*, *inordinate* muscular action, and *restlessness*. In *neuralgia*, *odontalgia*, and acute *rheumatism* it allays all *pain* as speedily as opium, and it often acts not only as an *anodyne*, but as a *soporific*." *

The evidence of the distinguished and lamented Drake on any subject of doubtful character from the American student must command the highest reverence and respect which can be accorded to any author of ancient or modern times. His testimony is especially valuable on this question, since it is the deduction not only of his own careful and numerous observations, but is also the result of personal conversation and consultation with nearly every prominent practitioner in the great valley of the Mississippi River. In his valuable work * he states:

---

* New Orleans Med. and Surg. Journal, ii. 290–300.

"*The Sulphate of Quinine.*—This medicine cannot be referred to the class of simple diffusive stimulants, such as capsicum or ammonia, which in large doses excite inflammation and fever; nor to that of tonics, as gentian and calumba and the carbonate of iron, for although in *minute* and regularly repeated doses it will, to a certain degree, excite and sustain the actions and energies of the system, these effects are by no means those which characterize it as a therapeutic agent. It has, perhaps, better claims to be admitted in the order of sudorifics, for increase of perspiration generally follows its administration, if the system and the regimen of the patient be favorable to such an effect. With greater propriety, however, may it be grouped with the *sedative* and *antispasmodic narcotics;* but not with the soporific division, for it does not, like opium, produce sleep. When its operation in *liberal doses* is noticed, it will be observed to diminish the frequency and spasmodic force of the heart's contractions; expand and soften the pulse; increase the functions of the skin, and tranquillize the innervation. Its sinister effects on the brain are vertigo, *tinnitus aurium,* and temporary hardness of hearing. The last is analogous to the effect of some other narcotics, as stramonium and belladonna on the pupil of the eye. In generalizing the phenomena which follow its exhibition in considerable portions, we may say that its action is directed more on the great sympathetic and the muscular system of the apparatus of organic life, generally, than upon the functions of animal life,—another point of distinction between it and opium. Two opposite conditions of the system contra-indicate its use: 1st, a high degree of phlogistic diathesis with arterial fulness; 2d, great depression of the vital forces.

---

* Diseases of the Interior Valley of North America, second series pp. 60, 61–106, 110, 125.

"Quinine is better borne in congestive remittents and intermittents than in any other form of fever. It is tolerated by the system as tartar emetic is tolerated in pneumonia and blood-letting in cerebral inflammation. I recently gave a negro boy, under twelve years of age, about fifty grains of quinine within twelve hours, without producing deafness or ringing in the ears. Its good effects, however, were none the less evident." "When the pulse, under the use of quinine, gets more feeble as it becomes slower, with a copious supervening sweat, I know of no remedy equal to carbonate of ammonia, the quinine being at the same time suspended."

In addition and in proof of the sedative and febrifuge properties of this invaluable agent, which have been attested by the authorities quoted, and many others,* we have to remark that its antipyretic action has been conclusively established by the *testimony of the thermometer.*[*] From its liberal employment in a vast number of cases of pneumonia, acute rheumatism, diphtheria, croup, scarlatina, erysipslas, and the various types and forms of miasmatic fever, the writer has observed the temperature to fall from its maximum to the normal degree and even below that in a few hours. This is a direct effect of the medicine. The idea that its sedative effects are the secondary results of primary excitation is clearly disproven by thermometric observations. The presence of fever, therefore, so far from contra-indicating its use, rationally invites its exhibition in doses increased in direct ratio with the elevation of the morbid temperature. On the other hand, its use in large doses should be avoided in those diseases and conditions in which the internal heat is below the physiological point. We do not wish to be understood as advocating the employment of quinine in all diseases attended with fever, but only in those in which its salutary action has been proven by ample and enlightened experience,—the only certain test of the value of therapeutic agents.

---

* Hester, New Orleans Med. and Surg. Journal, ix. 556. Anderson, Ibid., xi. 78. Mitchell, Ibid., x. 285. Tuck, Ibid., v. 719. Shanks, Ibid., xii. 195. Grier, Ibid., ix. 432. Brooks, Ibid., xi. 298. Lewis, Ibid., iv. 173. Monett, Amer. Jour. Med. Sci., xiii. 35. M. P. Scott, Stethoscope, Va., 11, 119. Webb, Ibid., 11, 173. Porter, Amer. Jour. Med. Sci., x. 307. Harney, Med. Statis. U. S. Army, 1839–54, p. 645. De Leon, Ibid., 673. Bell (Bell and Stokes' Practice), ii. 781. Harris, So. Jour. Med. and Surg., Charleston, ii. 628. Branch, Charleston Med. Jour. and Rev., iii. 167. Melier, Mém. Roy. Acad. de Méd., x. 565. See also Briquet, "Traité du Quinquinia," 48, for a long list of European authors.

---

[*] Bouchut, "Pathologie Générale," 2me ed., Paris, 1869, p. 954. Hirtz (Eulenberg, Briquet, Legroux, Wachsmuth), Nouveau Dictionnaire de Médecine et de Chirurg. prat., Paris, 1862, tome vi. 189. Jaccond, Pathologie Interne, Paris, 1870, tome i. 90. Wunderlich, Das Verhalten der Eigenwarme in Krankheiten, Leipzig, 1870, p. 138.

EFFECTS IN OTHER DISEASES.

We are indebted to M. Briquet for a series of observations in regard to the effects of the sulphate of quinine on the circulation in patients affected with *acute and chronic rheumatism* and *typhoid fever*, with the following results:

Chronic Rheumatism.—(1) Of thirty patients affected with this disease, in which but few, before the experiment, had any acceleration of the pulse, in six whose pulse was sixty (*one* took seventy-five grains of the salt in twenty-four hours) the pulse was reduced to fifty. In two who took less, the pulse was reduced to fifty-five, and in the rest there was no change. (2) In seven whose pulse before treatment was between seventy and eighty on the day *after* treatment, in *two* it was reduced to seventy-two, in two to *sixty-eight*, and in *two* to sixty-two and *sixty*. (3) In four whose pulse was from eighty to ninety, in *one* it was reduced; in another it was reduced to sixty-four. In two others, the pulse became more frequent. (4) In two whose pulse was from one hundred and ten to one hundred and fifteen, it was reduced to ninety-six and ninety pulsations per minute.

Acute Rheumatism.—This category comprised twenty patients, to whom the sulphate of quinine was administered in doses of seventy-five to ninety grains a day, and in whom the pulse averaged before treatment ninety,—one-third of them having the pulse at one hundred and more, and one-seventh at sixty. On the first day the average diminution of the pulse was eighteen and a half pulsations per minute. On the second day the mean decrease was twenty-two. On the third day the average decrease was twenty-six, and on the fourth day the mean decrease was twenty-six.

Besides these cases, the remedy was given to others in increased doses with corresponding results.

Typhoid Fever.—In forty-two cases the sulphate of quinine was given in doses varying from forty-five to sixty grains per day, with the following results: (1) The pulse declined soon after the administration in seven patients. (2) In four mild cases treated with thirty grains a day, the pulse fell from one hundred to eighty. (3) In nineteen grave cases, in which thirty to sixty grains were given, and in whom the pulse was at ninety-six on an average, it declined to seventy-eight. (4) In eleven cases of very grave typhoid fever treated with forty-five to sixty grains a day, and in whom the pulse averaged ninety-eight, it fell to sixty-eight. (5) In eight cases that died, who had had an average pulse of one hundred and four, and who took from forty-five to seventy-five grains a day, it fell on the second day to eighty-two, and on the third and fourth days to seventy-one.

It was observed in the typhoid fever cases, as in those of rheumatism, that the pulse was reduced more in those in which it had been most frequent. It very often happened that the influence on the circulation persisted several days after the cessation of the medicine, and in many cases the patients left the hospital with their pulses below the physiological standard.

EFFECTS ON THE BLOOD.

Although we have seen it stated by M. Melier, as the result of a few experiments, that the sulphate of quinine has a tendency to liquefy and diminish the coagulability of the blood, yet this conclusion has not been verified by the more extended observations of M. Briquet, who subjected the blood of patients and dogs to chemical analysis who had been subjected to the influence of quinine in large doses. As the result of his experiments and observations, the author arrives at the following conclusions:

1st. That the proportion of fibrine was always *increased* after the administration of large doses of quinine, and diminished after its discontinuance.

2d. That the relative proportion of blood-globules was diminished, a fact which he did not attribute exclusively to the salt. The diminution amounted to one-sixth and one-fourth.

3d. The quantity of the serum of the blood was slightly increased.

4th. That the administration of quinine or its salts has no appreciable influence on the salts of the blood.

MODE OF ABSORPTION AND ELIMINATION.

From the experiments of MM. Henry, Lannaux, Follin, Landerer, and Wöhler, it has been ascertained perfectly that the sulphate of quinine is rapidly absorbed into the blood. M. Landerer * has shown that after the administration of quinine it is found in the blood and excrement. He found it in the liquid urine and also in the yellowish-red sediments, which consisted of phosphate and urate of lime and carbonate of ammonia. He also examined the blood of patients suffering from intermittent fever, and who had been bled on account of inflammatory complications. The serum of the blood had a decided bitter taste, and when evaporated and the residue digested with acidulated water, the extract afforded quinine on being precipitated with ammonia.

---

* Chem. Gaz., i. 47, quoted in So. Jour. Med. and Phar., i. 461.

M. Henry* found quinine abundantly in the urine of dogs submitted to experiment, and also in the liver. M. Briquet has corroborated these statements in the most conclusive manner.

The rapidity with which quinine is absorbed is very great. M. Briquet detected it in the urine in a space of time varying from half an hour to an hour after its injection, and there is no doubt but this agent is principally eliminated by the kidneys. The rapidity of absorption is less in febrile diseases, and this fact leads to a therapeutic indication, viz., that the salt should be administered at a period sufficiently long before the expected paroxysm to insure its full constitutional effects.

---

* Mém. de l'Acad. Roy. de Méd., x. 739.

TOXICOLOGICAL EFFECTS.

When we consider to what a vast extent the sulphate of quinine is employed, and by how many unprofessional as well as unskilful persons it is administered, it is a matter of astonishment that comparatively so few serious results have been related. No stronger proof could be given, however, of the fact that it possesses less hurtful or dangerous properties than at one time were attributed to it. No authentic case within our own observation has occurred of dangerous, much less fatal, effects having been produced by it when given to man in health. We have seen that M. Bailly took himself one hundred grains without injury, and that M. Giacomini also took very large doses for several days without producing any serious permanent effects. The following case is an instructive and interesting example of its pernicious effects when taken in health in excessive quantity.

" A man from forty-five to fifty years of age having taken at a single dose about two hundred grains of sulphate of quinine by mistake for cream of tartar, was first seized with cardialgia, nausea, faintness, and entire inability to move. Eight hou after having swallowed it, Dr. Giacometti, of Mantua, who communicated this observation to Professor Giacomini, was called to the patient, whom he found in the following state: The temperature of the body was below the normal standard; his extremities cold; his lips and fingers livid, and his breath fetid. His respiration was slow and gasping; the pulse regular, but so feeble as to be hardly perceptible; his voice inaudible; the pupil extremely dilated, and his hearing and sight almost extinct. His tongue was not dry, but pale, and covered with thick and viscid mucus, and the patient was thirsty. After taking a stimulant potion, containing about thirty drops of laudanum, and friction having been made over the whole body, he became warm; the pulse became more perceptible; his respiration less slow, and his countenance more animated. The patient experiencing colicky pains and flatulence, an enema was given, which produced evacuations that relieved them. Soon his appetite returned, and on the fourth day treatment was discontinued. On the fifth day the patient could sit up for an half-hour, but he could not stand on his feet, so great was his prostration. The feebleness of hearing and seeing, although diminishing every day, did not cease completely for a long time. Finally the patient of Dr. Giacometti recovered." *

The following extraordinary cases are also found in M. Guersant's article (same volume and page): "M. Bazire, a physician at Martainville, on the Upper Seine, possessing an ardent and excitable imagination, had an unlimited confidence in the power of the sulphate of quinine, which he frequently employed in the intermittent fevers which reigned in the vicinity. He was strongly convinced that if this remedy sometimes failed, it was on account of its being employed in insufficient doses. Such was the conviction of the mind of our *confrère* when his wife was attacked with an intermittent, which he thought sufficiently grave to demand energetic treatment. In consequence, he gave her two hundred and forty grains of sulphate of quinine in a very short space of time. The patient soon fell into a state of stupor, with heaviness of the head, amaurosis, deafness, and difficulty in moving. M. Bazire, persuaded that these new symptoms were owing to an approaching invasion of another paroxysm, gave, in addition, three hundred and seventy-five grains of sulphate of quinine to his wife. After the ingestion of this enormous dose, the symptoms increased with fearful rapidity. The patient became entirely deaf and blind, her respiration was embarrassed, her pulse very bad, and her skin cold. It was necessary to have recourse to powerful revulsives, but the patient remained in a stationary condition for several days. Whilst this deplorable scene was passing, our unhappy *confrère* was in a state of great fatigue from attending a great number of cases of intermittent fever, which was epidemic. The reverses which he experienced threw him into despair; he saw, with affright, the disease triumphant and the power of the medicine which he believed infallible too often inefficacious. However, by a singular fatality, even these failures only increased his delusion in regard to the sulphate of quinine. To complete his misfortunes, he was soon attacked, himself, with intermittent fever, which gave the last stroke to his delirious imagination. He believed his disease to be of a pernicious type, and desired, in consequence, to double the dose, persuaded that he would surely triumph over the malady. He hastened, then, to administer to himself nine hundred grains of the sulphate of quinine by the mouth and by the rectum. The same symptoms which had been observed in his wife were manifested in him. He immediately lost his hearing and sight; his respiration became frequent, quick, and similar to that of a man affected with pneumonia terminating in hepatization. His pulse was small, irregular, and his limbs cold. In spite of this assemblage of formidable symptoms, and contrary to the advice of his *confrères*, the unhappy Bazire, the victim of a species of monomania, took in addition, in the space of eight or nine days, five ounces of sulphate of quinine. M. Réveillon was then summoned. He found him covered with a cold sweat, completely deaf, and blind; his respiration was difficult and rattling; he was in profound stupor, and his countenance resembled that of a drunken man. When one succeeded, with great difficulty, in making him hear, his answers were correct; but soon delirium supervened, and his respiration became more and more embarrassed, and M. Bazire expired. M. Réveillon was not permitted to make an autopsy. Madame Bazire only owed her life to the decease of her husband, which prevented him from attending her further; but her convalescence was extremely long; she remained for a long time deaf and blind,—and even at present her vision and hearing are extremely feeble."

---

* Dict. de Médecine, or Répert. Génl., xxvi. 568 (Guersant).

M. Recamier* has reported a case of death after the administration of sulphate of quinine in a case of acute articular rheumatism. This patient had been shortly before treated for smallpox, and there was "derangement of intelligence" before the medicine was given, and the patient labored under "general fever." M. Recamier having just witnessed an admirable cure effected in an analogous manner in a lady in private practice, resolved to employ the same treatment in this case. On the first day forty-six and a half grains were administered in twelve papers; one to be given every hour. No bad effect resulted. The second day seventy-seven grains of sulphate of quinine were prescribed, to be taken in the same manner. The patient had only taken fifty grains, when he was suddenly attacked with extreme agitation, followed by furious delirium, and death occurred in a few hours. No certain deduction can be made from the result of this case as to the share which the sulphate of quinine had in the unfavorable issue. The derangement of intelligence mentioned, *before the period of the administration*

---

* Amer. Jour. Med. Sci., v. 494; from Gazette des Hôpitaux, 1842.

of quinine, was very probably the result of incipient meningitis,—delirium of a "furious" character not being one of the effects of quinine, as we have seen above. We consider "the admirable cure" at once an offset to, and a practical commentary on, the unfortunate case.

M. Petit Jean,* another French physician, states that he has "frequently observed the influence possessed by the sulphate of quinine in procuring abortion in the part of the country where intermittent fevers were frequent. He, as well as others, observed that the salts of quinine in the dose of fifteen grains a day in many instances caused abortion."

From the results of an experience of forty years in the treatment of malarious fevers, we are confident that M. Petit Jean has mistaken a consequence of the intermittent fever for a result of the action of quinine. At the commencement of our career, when we were timid in administering quinine, abortion was no uncommon occurrence in pregnant women attacked with the various types of periodical fever, and to whom no quinine had

---

* South. Jour. Med. and Phar., i. 191; from Chemist, December, 1845, p. 544.

been given. It is a frequent occurrence in fevers of all descriptions, and the female may consider herself fortunate in passing through the commotion of any fever without a premature expulsion of the fœtus. Since we commenced to employ quinine in liberal, yet reasonable, doses in paroxysmal fevers, we have *never* observed abortion in patients affected with them. We should reasonably suppose that an agent which, when properly administered, would prevent the convulsive rigors of the cold stage, and the high febrile excitement of the exacerbation which follows, would be the best means of preventing abortion in those subject to such violent disturbing influences,—a hypothesis which extensive observation has fully confirmed.

The opponents of the use of sulphate of quinine in proper doses will derive but little assistance for the support of their views from the perusal of the paper of M. Melier,* "Sur les Propriétés Toxiques du Sulfate de Quinine." The cases cited were those in which no judicious practitioner would have erred, three of them being those already quoted from M. Guersant's article, in which the sulphate was given in doses of from one hundred and eighty grains to five ounces. M. Melier, himself, states in another paper* in the same volume that he cured an infant *six weeks* old, affected with convulsions, by giving six grains of the sulphate of quinine on the first day, four the next, and the same quantity on the day succeeding. These, according to our estimate, would be equivalent to doses of fifty to sixty grains in an adult, if not more. So that we are not surprised that M. Melier should refer to this last paper in his observations "Sur les Propriétés Toxiques," declaring, "On ne me suspectera pas, je pense, de vouloir diminuer la confiance que l'on *doit avoir* dans le sulfate de quinine, *l'agent le plus précieux, à mon avis, dont se soit jamais enrichie la thérapeutique.*"

---

* Mém. de la Roy. Acad. de Méd., x. 722.

It is astonishing to find that the sulphate of quinine, however, has been given in enormous doses without producing any serious effects. Drake informs us that "Dr. Fair, of Montgomery, Ala., told him of a patient who took an ounce in three days and recovered, and Dr. Heriart, of Plaquemine, La., knew of an old lady who took ten-grain doses every two hours, till an ounce was swallowed. No bad effects occurred, and she recovered.*

---

* Des Affections Intermittentes à Courte Période, op. cit., p. 555.

The following case, related by Maillot,† in which very large doses were given with the happiest effects, is interesting and instructive:

"*Fièvre quotidienne pernicieuse, comateuse.*—Muller, a soldier of the Third Regiment of Chasseurs, of a good, strong constitution, had been discharged from my service about a month when he again came under my care, on the 15th of January, 1835, in the afternoon. He was in the most profound coma. We could gain no information in regard to the commencement of his disease; his pulse was full, large, but not hard; the skin but little elevated above the natural temperature; the respiration deep. His countenance resembled that of a man asleep, and he was altogether insensible to pinching and pulling his skin. (Diet, lemonade; venesection fifteen ounces, thirty leeches over the track of the jugulars; a quart of amylaceous opiated enema with sixty grains of sulphate of quinine, and forty grains of sulphate of quinine given by the mouth, two blisters to the thighs, and two sinapisms to the legs.) At eight o'clock in the evening, the coma was very profound; the insensibility, however, was less perfect, and his skin was warmer; bleeding from the temporal artery eight to ten ounces; forty grains of sulphate of quinine to be taken in two doses in the space of two hours; cold fomentations to the head. January 16, morning: The tongue is slightly indicative of gastritis, but the epigastrium is painful on pressure. The expression of the face continues somewhat stupid; the mind is, however, clear; he has had an abundant sweat during the night. The patient related to us that before his return to the hospital he had had five paroxysms of fever, which returned every day at three o'clock in the morning. It was during the fifth access that he was brought back to the hospital. The first paroxysms were accompanied by violent pains in the head and efforts to vomit. Diet, lemonade; forty grains of quinine to be taken immediately in one dose, cataplasms to the epigastrium, continue cold applications to the head. Complete intermission of fever took place during the day, and in the evening the patient was in the most comfortable condition. January

---

* Dis. Int. Valley of N. America, 2d Series, 91.

† Traité des Fièvres Intermittentes, 397.

17, morning: Apyrexia complete, no cephalalgia or thirst, epigástric pain increased, no lassitude in his limbs, no alvine discharge for several days. (Diet, lemonade; twenty-four grains of sulphate of quinine in an emollient lavement.) January 18: Convalescence. The 27th, the patient took half-diet, but he gradually resumed his usual diet. In the early part of February he had a relapse, which retarded his cure, but this was soon relieved."

M. Maillot concludes his description of this case as follows: "One hundred and eighty grains of sulphate of quinine here were administered in a few hours. One will search in vain among authors for examples of such medication. I leave to experience the charge of deciding upon its value. It is only by facts that questions of this nature ought to be decided. Theories are broken to pieces by facts which convince us in spite of ourselves."

I have myself witnessed similar examples to that related by Maillot; I have seen two hundred and forty grains given to a patient in twenty-four hours, who, at the commencement of its administration, had high fever, was in a state of comatose delirium, and who had every symptom of congestion and irritation of the brain; his eyes were injected and the temporal artery so distended with blood that its branches could be easily seen at a distance from the patient. Before one-half of the medicine was given every symptom of fever and cerebral disturbance had disappeared, and rapid convalescence ensued. His vision was not affected by the quinine, but for several days his hearing was impaired. This partial deafness, however, entirely disappeared before a week expired. Ten years afterwards he was in good health, when I lost sight of him. A few hours before the administration of the quinine, the patient was bled sixteen ounces from the temporal artery and cupped freely over the mastoid region, with partial relief of the head-symptoms.

Dr. T. J. Mitchell * relates a case in which his son, Dr. B. Rush Mitchell, gave two hundred and forty grains of sulphate of quinine in four hours with no development of bad symptoms, and followed by complete restoration to health.

Dr. F. A. Bates † states: "I have frequently given one huudred grains of sulphate of quinine

---

* N. O. Medical Journal, iii. 20.

† Ibid., vi. 187.

in a few hours, without any other complaint than a little ringing in the ears."

Dr. Ames * states that he recently gave to a negro boy under twelve years of age about fifty grains of sulphate of quinine within twelve hours, without producing any deafness or ringing in the ears. Its good effects were, however, none the less evident.

Dr. R. D. Webb † observes "that though raised in a country stigmatized as the hot-bed of malaria and resided two years in a Southern hospital where quinine was given freely, he had never observed any of the deleterious effects attributed to it;" and adds, "I knew a case occurring in the practice of Dr. Smith, of Alabama, in which half an ounce was taken in a single day without any unpleasant consequences."

Dr. R. G. Wharton,‡ of Grand Gulf, Miss., in an article on congestive fever, says that he gave half an ounce of sulphate of quinine in a bad case of that disease with perfect success, and that there was no deafness or headache following.

---

* Lewis's Med. Hist. of Ala., N. O. Med. Jour., iv. 173.

† Stethoscope, Va., ii. 176.

‡ Amer. Jour. Med. Sciences, vii. 343.

Our object in citing these examples, which might be greatly multiplied did space permit, is merely to show in what enormous quantities the drug may be taken without producing serious consequences. As we shall see hereafter, we do not approve the practice of giving such excessive doses.

In the fatal examples there is a remarkable agreement in the accounts of various authors in regard to the symptoms produced by quinine, viz., deafness, blindness, insensibility, failure of the pulse and coldness of the skin,—all the results of the depressing and other peculiar powers of the medicine. Let us now examine the symptoms clearly the result of the pernicious action of the sulphate of quinine, and endeavor to ascertain in what manner they are produced.

Tinnitus Aurium and Deafness.—These symptoms are usually attributed to congestion of the brain. I do not think so. We have seen that the most potent remedy for relieving congestion of the brain, both of an active and passive character, has been found in the salt itself. If it possessed the property of unduly exciting or unduly determining the blood to that organ, we should have witnessed accidents of that kind without number. It is therefore evidently a peculiar and specific effe of the medicine, only *hurtful* and *permanent* when induced by excessive doses.

TINNITUS AURIUM is often induced by the smallest dose of the medicine, and usually ceases promptly after the withdrawal of the remedy. It is an unpleasant and annoying symptom to the sick, and constitutes usually the greatest objection the patient has to its reception. A few instances of permanent deafness have been recorded. In my prolonged experience I have never observed it, but as it may be produced by the sulphate of quinine when given in too large quantities, it certainly in itself alone is a great objection to its use in inordinate doses. Blindness has been very rarely observed, either as a temporary or permanent effect of the sulphate of quinine. I have never known a single instance as the result of its use. It has never, I believe, been the effect of any reasonable dose of the medicine. It is evidently the result of paralysis of the optic, as deafness is of the same condition of the auditory, centre.

Conclusions in Regard to the Physiological Action of Sulphate of Quinine.—1st. It is incontestable that slight and transient perturbation of the nervous system and circulation are observed soon after the ingestion of the sulphate of quinine when given in small and repeated doses. This, however, is not always observed. This temporary effect has led to its classification by writers on the Materia Medica and Therapeutics among tonics and stimulants. It is evidently due to its local action upon the mucous membrane of the stomach.* The sulphate of quinine, like all other substances which are absorbed into the blood, has necessarily to undergo the process of absorption. The presence of any ingesta in the stomach excites the functions of that organ in more or less degree. The chemical and vital processes of digestion being called into play, excite the functions of the brain and stimulate contractions of the heart by reflex action. To the healthy stomach, quinine cannot be considered as possessing the properties of an irritant, except in a slight degree; when, however, the mucous membrane of that organ is inflamed, experience amply proves that its local action upon it is that of an *irritant.* It is probable that the irritant effects of the sulphate upon the stomachs of some persons, apparently enjoying health, is due to a susceptibility dependent upon a condition of the mucous membrane not strictly physiological.

---

* This is proven by the fact that when introduced hypodermically there is no period of excitement.

2d. The sulphate of quinine, in large doses or in small doses, frequently repeated after the temporary stage of perturbation above described, exerts a calming and sedative action upon the nervous system and circulation. This has been clearly shown from the facts we have arrayed. 1st. From experiments on animals. 2d. From its effects on man in health; and 3d. From its effects in diseased conditions of the animal economy. The quantity necessary to produce sedation is variable, according to the age or susceptibility of the subject.

3d. Given in *excessive* doses, it reduces the actions of the nervous and circulating systems far below the physiological state, and in sufficient quantities it paralyzes in a great or less degree the action of the heart, the cerebro-spinal and ganglionic nervous system, and in rare cases may produce death.

4th. In large doses, the sulphate of quinine produces sleep and relieves pain.

5th. In large doses, the sulphate of quinine exerts a marked effect on the calorifacient function, reducing the temperature of the body in health and disease.

These conclusions are not only sustained by the facts already given, but will be still more clearly demonstrated when we shall treat of its application in the treatment of particular diseases.

An agent possessing the properties above enumerated must necessarily possess a wide range in its application to the cure of disease, but in the present condition of pathological science the propriety of the administration of any article can only be determined by numerous and repeated experiments. The essential nature of many diseases remains to be discovered, and probably will forever be enshrouded in mystery. No theory of disease yet promulgated, and no classification yet made of medicinal agents, has led to any positively definite system of therapeutics, and the applicability of remedies to the treatment of disease can only be positively ascertained and determined by experience.

ON THE THERAPEUTIC USE OF SULPHATE OF QUININE.

The curative effects of the sulphate of quinine in *simple ague* are so well known and appreciated, that it will be unnecessary to devote much space to its consideration. No agent yet discovered has been found so certain in its effects. Given in small and repeated doses in the intermission, or in large doses a few hours before the expected access, it arrests the disease promptly and surely. In many thousand cases I have never seen it fail when given in proper quantity. I trust that the examples which have been given of its use in enormous doses, not having been followed by serious or permanent ill effect, will tend to diminish all hesitation in employing this remedy in sufficient doses. Thirty-five grains of pure sulphate of quinine will arrest the paroxysms of intermittent with a degree of certainty to be found in the history of no other remedy. I do not remember a single example of its failure to prevent the recurrence of the cold stage, when given in that quantity, except where it had been administered too late to undergo absorption and to produce its full effect.

In simple intermittent, I prefer to give that quantity in divided doses. It is tolerated with more ease by the stomach, and produces its salutary effects with less discomfort to the patient. When the intermission, however, is very short, it may be given in full quantity at once. Should it produce any unpleasant effects, they are not to be compared in severity to the agony of a febrile paroxysm. After the paroxysms are arrested, its use should be continued in divided doses, gradually lessened in quantity, for two or three weeks. The relapses of intermittents, which so frequently occur, may thus be generally prevented.

The prophylactic powers of the sulphate of quinine are generally conceded. Numerous experiments have established the capacity of the article beyond the reach of cavil.

The salutary effects of quinine may be essentially assisted by other therapeutic measures. The advantage of previous evacuation of the alimentary canal is generally recognized. By this means all offending matter is removed and the absorption of the salt facilitated. When, however, the intermission is very brief, or the practitioner is called too late, the remedy should be administered without delay.

In Remittent Fever.—The employment of the sulphate of quinine in remittent fever has been the subject of much controversy, but has gradually become more general since its sedative powers have been more fully recognized. As a proof of its efficacy and safety, we may merely state that it is almost universally employed in this disease by those who have had most frequent opportunities of observing it in its most violent and malignant forms.

In the ordinary form of remittent fever, I have adopted the following practice during the last forty years with *invariable success* in several thousand cases.

Active measures will be found usually unnecessary during the chill, as the vital powers are fully competent to produce reaction. I disapprove the method of torturing the patient with heavy bedclothes and hot applications, but consult his feelings in regard to them, and allow cool drinks in moderate quantity.

IN THE EXACERBATION, if the pulse is hard or full and resisting, especially if attended with intense cerebral or spinal pain, a moderate bleeding from the arm will produce generally great relief, *but this will be very rarely necessary* in the present adynamic medical constitution. Local bleeding will usually be found sufficient, and is an invaluable adjunct. Leeches to the temple, or cups to the occipital or spinal regions, may be freely applied, as the determination may indicate. If nausea and vomiting or other symptoms of gastric irritation be present, leeches or cups to the epigastrium will be followed by great relief; and if these means should be succeeded by a simple enema, under their conjoined action the bowels will gently respond, and add greatly to the comfort of the patient. Cold drinks, ice, the effervescing draught and lemonade may be freely allowed. Under this treatment the patient will find great alleviation from suffering, and the intensity of the fever will be usually diminished. At bedtime—say at nine or ten o'clock at night—it is almost our invariable rule to administer a cathartic dose of calomel and rhubarb, composed of ten or twelve grains of each. At some period before or after midnight the fever will generally be found more or less to decline. We prefer this period for the administration of the principal remedy, because our experience teaches us that it is then better borne and produces its salutary effects in a more decided and complete manner than at any other time. We, however, whether the fever has declined or not, then administer fifteen to twenty grains of the sulphate of quinine in a single dose in pills, in a gelatin capsule, or diffused in a wineglassful of cold water. We regulate the dose by the degree of fever present. If it is intense, we administer the large quantity; if very moderate, less will answer.

Under the combined action of the cathartic and quinine, free evacuation of the bowels will usually occur, but rarely excessive. Three or four hours are now suffered to elapse, during which the topical bleeding is repeated if the local symptoms do not yield. The condition of the patient will now be found generally much improved. The cerebro-spinal pain is either removed or mitigated, the pulse less frequent and more soft, the skin relaxed and moist, and the gastric irritation subdued. We therefore repeat the quinine in diminished doses of five or six grains every three or four hours until the period of chill has passed, generally exhibiting altogether from thirty-five to forty grains before that time. In cases attended with much gastric irritation or diarrhœa, the addition of a full dose of opium, say one and a half or two grains with ten or twelve grains of the submuriate of mercury at bedtime, instead of the rhubarb; this forms an excellent combination, which will enable the stomach to retain the quinine with more certainty. If the stomach should not tolerate it, however, it must be given by the rectum or skin.

Under this simple plan of treatment, remittent fever as it usually appears is certainly and safely arrested. Owing, however, to the peculiar liability of the affection to relapse, or terminate in protracted intermittent fever, we usually continue treatment. We think it advisable to prescribe calomel or blue mass for two or three successive nights in aperient doses, followed by eight or ten grains of quinine on the succeeding mornings. In cases attended with coma, delirium, or convulsions during the exacerbation, topical bleeding will be freely required and the application of ice or cold fomentations to the head. We have, however, been more gratified with the effects of the *cold douche* in these applications than with any other remedy. A full dose of calomel should be given as soon as practicable, followed by a stimulating enema. In mild cases, however, it will not be necessary to resort to very active treatment, as these symptoms gradually yield with the subsidence of the paroxysm.

In the ALGID FORM of intermittent and remittent fevers the following treatment is recommended:

IN THE COLD STAGE, external means are all-important. Warm applications are to be assiduously made to the parts reduced in temperature, together with stimulating frictions. These should be freely applied to the whole length of the spinal column and extremities. A large blister should be placed over the epigastric region, and if the head is affected, another should be applied to the nape of the neck. To produce reaction along with these applications, I prefer enemata of the sulphate of quinine. Ten grains may be thrown up the rectum every half-hour until reaction ensues. If diarrhœa is present, laudanum should be added to the enema. If this is not retained, the hypodermic injection must be resorted to. By these means cases apparently hopeless have been rescued from death.

During the EXACERBATION the reaction is sometimes intense. When this occurs, I have ventured on the abstraction of blood from the arm in moderate quantity with decided benefit, but this is seldom necessary. The case now requires only to be treated as the ordinary form, save with perhaps a more liberal use of quinine. A moderate dose of calomel (ten or fifteen grains) alone or combined with one or two grains of opium, if there is much gastric irritation or diarrhœa, is followed in two or three hours by a full dose of quinine, say twenty grains, and repeated in doses of five to ten grains every three or four hours until thirty-five or forty grains are taken. The medicine should be so given that the last dose may be taken two or three hours before the expected paroxysm. I have never seen a chill or cold stage recur after forty grains of Farr's (now Powers & Weightman's) sulphate of quinine had been exhibited in sufficient time for its effects to be fully induced. Although the patient may be generally considered beyond danger when the paroxysms have been arrested, yet I esteem it to be good practice to prevent relapse by placing the patient on a gentle alterative course, and to repeat the quinine in diminished quantity for several weeks thereafter.

Quinine is often defeated in its action by the presence of gastric irritation and inflammation. In such cases it may be given by the rectum. When the intestinal mucous membrane is also in a state of phlogosis, the remedy may be employed hypodermically.* Its effects, when administered in this manner, are prompt and decided. Besides, in the algid form, the sulphate of quinine has been found no less indispensable and valuable in the other varieties termed *proteiform* by Morton,* and *pernicious* by Torti,† and described by Werlhoff,‡ Burserius,§ Senac,‖ Cleghorn,¶ Chomel,** Bailly,†† Maillot,‡‡ Gintrac,§§ and others in Europe and many writers in our own country. To the illustrious Torti we are perhaps indebted more than to any other author for a knowledge of the value of cinchona in those fatal varieties of malarial disease. Under the heads of *cholerica, dysenterica, subcruenta, atribiaris, cardiaca, diaphoretica, syncopalis, algida, subcontinua, malignans, legarthica,* etc., he described those fatal manifestations of the action of the same morbific agency, in which the wonderful powers of the bark were clearly and fully demonstrated. To these varieties or forms many others have been added by subsequent writers. The different modifications of treatment in these various local expressions of the same morbific cause it would be impossible to detail within the limits of an essay. It is sufficient to add that the transition from the employment of the bark to the substitution of quinine was a *natural* and *inevitable change* in the *practice* of those who had wisely followed the admonitions of the illustrious Italian physician. At present there is but little contrariety in the practice of enlightened practitioners in regard to the employment of quinine in the *most malignant* and *rapidly fatal varieties* of malarial disease. However writers may wrangle about the proper methods of treatment in other forms, yet in Pernicious Fever they *unanimously* accord to it the most exalted virtues. Yet in these forms there is usually *no remission* of the fever or other symptoms until death claims its victim. Though here we perceive the deepest implication of *vital organs,*—indisputable evidences of congestion and inflammation of the brain, spinal marrow, lungs, stomach, bowels, liver, and spleen,—indeed, though "the life of all the blood be touched corruptibly," yet by the *bedside*, in the stern presence of impending death, they waive their strife, they forget or ignore their speculations in regard to this agent *exciting inflammation*, *increasing congestion*, and *liquefying* the *blood*, and *boldly* give a remedy which they have *denounced* for having produced the very evils, in *milder* forms of the same disease, which they *implore* it to *avert* when present in *aggravated degree.* The inconsistency of those who deny that quinine is a sedative antipyretic is here evident.

---

* The following is the excellent formula of M. Dodeuil for its hypodermic use:

Distilled water, 20 parts;
Sulphate of quinine, 2 parts;
Tartaric acid, 1 part.

One-third less than the usual dose of quinine is required when given by the skin.

---

* Opera Medica (De Proteiformi Int. Febris), Lugduni, 1737.

† Therapeutice Specialis ad Febres Perniciosas, ii. 1, Leodü, 1821.

‡ Opera Medica, Hanoveræ, 1775.

§ The Institutes of the Practice of Medicine, translated by Wm. Cullen Brown, Edinburgh, 1800.

‖ De Recondita Febr. Int. tum Remit. Naturæ, Amstelodami, 1759.

¶ Observations on the Epidemical Diseases of Minorca, London, 1768.

** Des Fièvres et des Maladies pestilentielles, Paris, 1821.

†† Op. cit.

‡‡ Op. cit.

§§ Pathologie interne, Paris, 1853, iii. 770.

We conclude our observations on the employment of the sulphate of quinine in periodical fever with the following suggestions:

1. As the chief danger in this class of diseases is to be apprehended from the recurrence of the paroxysms, and as experience has proven that the medicine may be safely given at any stage of the disease, it is our duty to arrest the disease as soon as practicable by its immediate administration.

2. The sedative and febrifuge effects of the medicine may be assisted by other remedies which have proven to be efficacious. Thus in-

tense febrile heat may be moderated and inflammation may be combated by such methods of treatment as may be found applicable. The action of quinine is by no means disturbed by the remedies of inflammation, such as bleeding, veratrum, tartar emetic, mercury, etc.; on the contrary, it is aided by them in the production of its salutary effects. Where the impression of mercury is desired, the sulphate of quinine is a powerful promoter of its development.

3. When given in the presence of fever, it should be administered in such quantities as to produce decided sedative action, and to prevent the next exacerbation with certainty. I regard fifteen grains of the medicine as the minimum certain sedative dose for an adult, to be repeated as occasion may require.

4. Bearing in mind the sedative and depressing effect of the remedy in large doses, its use is contra-indicated in those conditions of the organism in which the powers of life are already below the physiological standard. In these states the sulphate should be given in small doses.

In Neuralgia.—In illustrating the effects of sulphate of quinine in disease, its therapeutic use in neuralgia was necessarily noticed in cases when it evidently arose from the same cause as that producing periodical fever; but there is every reason to believe that it has been found as equally useful in cases of neuralgia which could not be traced to any miasmatic source, and assuming either a periodical or continuous type.

In *neuralgia* of the nerves of the *ganglionic system*, the paroxysms are usually *less regular* and *distinctly periodical* than those of the *cerebro-spinal system.* This is due, in the opinion of M. Jolly,* to the fact that the ganglionic nerves are distributed to organs whose functions are of a more continuous character, and if the lungs, stomach, etc., exhibit periodicity more evidently, it ought to be attributed to the fact that these organs are partly under the cerebro-spinal influence.†

The march of ganglionic neuralgias also, according to M. Jolly, is different from that of those of the cerebro-spinal system. The latter manifest themselves chiefly in the afternoon or night, and cease at the approach of day. Ganglionic neuralgias usually commence in the *morning* or after *midnight*. Interesting examples of various forms and types of neuralgia which yielded promptly to the action of cinchona and its salts may be found in the works of various writers, to which reference may be found below.*

---

* Dict. de Méd. et de Chirurg., xii. 19.

† The writer takes pleasure in referring the student to the admirable essays on this and kindred subjects by our countryman, Dr. H. F. Campbell, of Georgia, in the Transactions of the Amer. Med. Association, and especially to his prize essay on the Excito-Secretory System of Nerves, vol. x. p. 465.

In Yellow Fever.—As by many practitioners the bark was employed and recommended in the cure of yellow fever, the administration of the sulphate of quinine succeeded as a natural sequence. The different opinions in regard to its effects would seem to indicate that in some epidemics the medicine has proven highly efficacious, whilst in others it has been found injurious or nugatory.

According to Dr. Drake, Dr. Dodd "may be justly regarded as the first to establish the safety of this practice" in this country.†

---

* Morton, Opera Medica, obs. xxvii. Senac, op. cit., 136. Van Swieten, Comment. on Boerhaave, vii. 218, 219. Sauvages, Nosologie, i. 461. Senac, op. cit., 75, 78. Chomel, Des Fièvres, 412, 413. Mongellaz, Monographie des Irritations Intermittentes, 207–18. Bonnet, Fièvres Intermittentes, 137–44. MacCulloch, ii. 169. Holland, Med. Notes and Reflections, 241–46. Drake, Diseases Int. Valley N. America, 2d Series, 182, 183.

† Dis. Int. Valley N. A., 338.

In the epidemic at New Orleans, in 1839, Dr. Mackie instituted experiments with it with the most decided salutary results. Dr. Harrison speaks enthusiastically in favor of its effects in the yellow fever of that year in that city, and states, "the fever, in most cases, was cut short as if by enchantment;"* and its employment has also been highly lauded in other epidemics by Drs. Cummins,† Batcheler,‡ W. H. Andersons,§ Shanks,|| Stone,¶ and others.** On the other hand, in other localities, the treatment of yellow fever by quinine has signally failed in arresting the disease or diminishing its mortality. According to the testimony of Dr. Lewis,†† it signally failed in every form of yellow fever in Mobile. Of this treatment in an epidemic of this same disease in the same city, except "in a few intermittent cases, which are seen in every epidemic," Dr. Nott‡‡ remarks that it was utterly useless. In the terrible epidemic which raged at Norfolk and Portsmouth, Va., I believe that it is generally conceded that the quinine practice, like every other mode of treatment, was found ineffectual.

---

* N. O. Med. and Surg. Journal, ii. 332, 1845.

† Ibid., x. 352. ‡ Ibid., x. 404.

§ Ibid., xi. 86. || Ibid., xii. 705.

¶ Va. Med. Journal, v. 481.

** See Drake, op. cit., 338, 342, and Briquet, op. cit., 442.

†† N. O. Med. Journal, i. 427.

‡‡ Charleston Med. Jour. and Rev., iii. 16.

We, perhaps, ought not to close our observations on the employment of quinine in this disease without quoting the following from Drake,* who had the advantage of personal consultation with the most eminent and successful practitioners in regions where yellow fever is habitually endemic:

"It is undeniable that the quinine has proved beneficial in the practice of a number of our physicians; but can it be regarded as a specific even in the modified sense in which it is a specific in autumnal intermittent fever? I think not; for in the hands of several physicians it has not produced any decided benefit, and all who have used it extensively have seen patients die with black vomit after their system had been thoroughly brought under its influence. Indeed, of its value in yellow fever, unmodified by any autumnal intermixture, we have not any satisfactory proof.

---

* Op. cit., 341, 342.

Nevertheless, so many epidemics present a mixed character, that even limited to them, its importance is very considerable. When no alliance of this kind exists, I am disposed to believe that it may shorten the stage of excitement, if exhibited in large doses immediately after copious depletion. Its narcotico-sedative effects on the nervous system of animal life, and the *centrifugal determination* of the *blood*, which it favors, as is shown by the *diaphoresis* which follows its exhibition, are well fitted to extinguish the morbid excitement. But in pure yellow fever, is this the subdual of the disease? It would seem not; for after the patient has lain for two or three days under its influence, in what Dr. Lewis calls the 'state of calm,' collapse, black vomit, and death may happen. There is, then, an insidious lesion of the system which it does not reach,—a root of malignity which it cannot eradicate. In the treatment of the most dangerous intermittents—either inflammatory or congestive—it does not display this impotence; for after its impress on the system is established, no ulterior fatal symptoms need be apprehended. The *third stage* of *yellow fever* is *not*, in fact, the same pathological condition as the *apyrexia* of an *intermittent*. It ends in health or collapse and death, while the apyrexia of the intermittent never terminate in health or death, but in a new paroxysm. We should not, then, be surprised at a difference in effect of the sulphate of quinine in the two cases; nor at the small degree of success which has as yet followed the efforts to ward off the collapse of yellow fever by treating its third stage with the quinine."

In Typhoid Fever.—To the physicians of the present generation, engaged in practice forty years ago, typhoid fever was almost a new disease, and as at that period the free employment of quinine in the various forms of periodical fever was attended with the most beneficial results, numerous trials were soon made with it in the first-mentioned disease.

Residing in a region in which the treatment of malarial diseases constituted the principal part of my practice, the advent of typhoid fever was so gradual and insidious, and it was also so disguised in its features by being mingled with those of the paroxysmal endemic, that it was some time before the new-comer was clearly recognized. It seemed at first to be so controlled by the dominating influence of malaria, that many cases assumed the intermittent, though more often the remittent type.

In these cases the effects of the sulphate of quinine were of the most gratifying character. But gradually the typhoid element predominated in its turn, and where before intermittents and remittents annually reigned, the typhoid fever was almost alone observed. The treatment by the liberal employment of quinine was, however, continued, and though its physiological effects were, in the majority of cases, fully displayed, and the febrile movement, the ever-attending cephalalgia and elevated temperature of the skin were lessened, and in some cases removed, yet, to our chagrin, too often the pyrexial phenomena after the effect of the remedy subsided again returned, and the disease pursued its usual protracted career.

Of the comparative success of the quinine treatment and the expectant method adopted by others, I cannot speak in positive terms, not having any statistics to guide me to a certain conclusion, but that it diminished the mortality in the first epidemics when it was intermingled with periodical fever, I entertain no doubt. Employed early, in the forming stage, it certainly diminished the violence of the febrile symptoms in the most intense grades of typhoid fever, when uncomplicated with any other disease, and in som epidemics, as I believe, it materially shortened its duration.

In Paris the sulphate of quinine was administered in typhoid fever with beneficial results by MM. Jacquot,[*] Worms,[†] Leclerc,[‡] Pereira,[§] Champaux,[||] and others, yet the treatment never became generally adopted, and as an exclusive method I believe it has now but few advocates. The following conclusions deduced by M. Briquet from the treatment of numerous cases by himself and M. Blanche are interesting and suggestive:

"1. The employment of the sulphate of quinine should not be considered a general and common method of treatment in typhoid fever. This medication is only applicable to certain special cases, and perhaps to certain epidemics. Commonly, it ought only to be employed to combat certain forms of the disease, and certain predominant symptoms. For this reason the sulphate of quinine should only be employed temporarily, and not beyond the eighth day.

---

[*] Archives Gén., xv. 5.

[‡] Abeille Méd., xiii. 211.

[‡] Ibid., 321.

[§] Thèse, 1842.

[||] Thèse, 1846.

"2. The most apparent effects of this medication are produced on the circulation, on the calorification, and the symptoms arising from encephalic disorder. Thus the fever is influenced in an undoubted degree in regard to the frequency of the pulse and the temperature of the skin, consequently we may diminish one of the most annoying symptoms to the patient, prevent congestions and visceral inflammations, which, according to M. Louis, are so easily produced by the continuance of the febrile state, and, in short, exercise a direct but very powerful effect on the symptoms which arise from excitement and congestion of the brain. Consequently, also, the employment of the sulphate of quinine, which is advisable when the fever is very intense and the temperature of the skin greatly elevated, will not be proper when the pulse is not very frequent and the temperature of the skin but slightly increased.

"According to the modification of the circulation which it manifests, it also produces a notable change in the phenomena arising from the encephalic lesion.

"Thus in all cases where these are predominant, the sulphate of quinine will be a potent means to relieve them, and when they are present in an intense degree (except in cases of prostration) it ought to be administered.

"3. The sulphate of quinine, then, principally succeeds in cases where the excitement of fever is accompanied with cephalalgia, titubation, agitation, and delirium; when the eye is bright, and complexion heightened; when, in short, the fever assumes a phrenitic or ataxic character. On the contrary, where there is prostration, stupor, *decubitus dorsalis*, a continual tendency to sleep and a comatose state, the sulphate of quinine, which promptly and notably increases these symptoms, should be avoided.

"4. Typhoid fever, accompanied with distinct and regular remissions and intermissions, may be favorably influenced by the sulphate of quinine, employed according to the method used in intermittent diseases.

"5. Lastly, either in consequence of the difficulty of absorption, or on account of the obtuse sensibility of the encephalon, the sulphate of quinine may be given without the least inconvenience in larger doses in typhoid fever than in any other disease. However, doses of fifteen to twenty grains are sufficient in mild cases. In those which are more severe, the dose should be increased from twenty to thirty grains, and finally, in cases of the gravest character, forty-five to sixty grains may be given per day." *

MM. Rilliet and Barthez,† in the typhoid fever of children, have administered the sulphate of quinine with beneficial effects. As the result of their employment of this agent they arrived at the following conclusions:

"1. The pulse abated in a notable manner, and also diminished in volume, but became irregular.

"2. The animal heat diminished at the same time that the pulse was reduced.

"3. In some patients the sulphate of quinine caused eruptions of sudamina and very abundant sweats at a period when they do not ordinarily appear in typhoid fever.

"4. In some cases desquamation of the cuticle occurred, similar to those following vesicatories.

"5. As negative effects, they did not observe any exasperation of the abdominal symptoms, or of the anatomical lesions which characterize the typhoid affection, and, in particular, that it did not produce enteritis."

---

* Traité Thérapeutique du Quinquina, 441.

† Maladies des Enfants, ii. 414.

The quinine treatment in other hands has not been attended with such favorable results. In 1843 the French Academy of Medicine,* to whom the Memoir of M. Broqua was presented, decided "that its beneficial effects had not been proven." Unfavorable reports of its action have also been made by M. Petit † and Drs. Peacock ‡ and Barclay.§

In concluding our notice of the effects of sulphate of quinine in typhoid fever, it ought to be borne in mind that that disease has proven rebellious to all methods of treatment proposed, and that there are more positive proofs of the efficacy of quinine than have been presented by others in favor of any other remedy or plans of treatment adopted for its cure. Shall we, then, abandon its use altogether? Shall we hesitate to have recourse to a remedy so potent under other circumstances, and especially in those fatal epidemics sometimes observed, when the expectant method can certainly point to no triumphs? That in judicious hands and accompanied with proper adjuvants, the sulphate of quinine, employed at the inception of the disease, may break the force of the attack and obviate the tendency to death, we are fully convinced. Can the same be attested concerning any other remedy in this disease? Let the opponents of its exhibition, at all times and under all circumstances, take care that in steering their precious freight of humanity so carefully afar from Charybdis that they do not become wrecked upon Scylla. The applicability of a medicine to the treatment of a disease cannot be determined in a day or a year, as may be witnessed in the history of the use of quinine in the present century. Less than twenty years ago the most distinguished teachers of medicine denounced its employment in the ordinary remittents of our country, unless there was an evident and distinct remission of fever, and the result was that the most fertile sections of our land remained a vast cemetery. Who can compute the lives lost as a consequence of the error? I do not pretend to say that the administration of quinine will ever be attended with as successful results in typhoid fever, or in any other disease, as time has proven it to be in malarial fever, but I do hold that it is unphilosophical to condemn it entirely without an appeal to further trial.

---

* Bulletin de l'Acad., viii. 624.

† Abeille Médicale, xiii. 241.

‡ Med. Times and Gazette, 1856, pp. 3, 55.

§ Ibid., 1853, p. 31.

As we have already intimated, typhoid fever, when occurring in localities where miasmatic or periodical fever is epidemic or endemic, becomes intimately blended with the previously dominating disease of the locality. Such cases have been termed typho-malarial fever. We have here a combination of dangers to contend with, and there is no doubt that the complication increases the gravity of the situation in a high degree. *Here* the employment of quinine is *indispensable*, and though it may fail in arresting the typhoid affection, yet it will *eliminate the malarial element* and render the treatment of the former malady more successful. It is well known to all experienced practitioners, that it is very often impossible at first to diagnose between typhoid and malarial fevers. We cannot wait and watch the course of the disease to decide its nature, for the delay may be hazardous in the extreme, consequently it has been our rule for many years in doubtful cases to give the remedy boldly and immediately. It will mitigate the symptoms if the case be one of typhoid fever, and cannot do harm unless it is continued too long. If it is a case of malarial fever, in from twenty-four to forty-eight hours the disease will be arrested. Quinine, in *this exigency*, is the *surest and safest method of diagnosis.*

In Typhus Fever.—Since the time of Morton, cinchona had been employed by English and Continental physicians in typhus fever, but not with a view of suddenly arresting its course.

In 1851, Dr. Dundas, of Liverpool, introduced the practice of giving large doses of quinine in this disease, and his example was soon followed by others. The plan adopted by this physician is thus related by him: * "The dose should be large—ten or twelve grains—and repeated at intervals not exceeding two hours. Three or four doses will, in most cases, be sufficient to exert the specific influence of the medicine, which is displayed by the dizziness of the head and tinnitus aurium, or in the rapid subsidence of all the urgent symptoms. In the latter event, three grains of quinine, or some bitter vegetable infusion, should be administered three times a day, and the patient supported with some good beef-tea, or other light nutriment, and wine, if necessary. Slops should be avoided, and purgatives also, unless obviously indicated, but an emetic of tartarized antimony when the *prima via* is loaded, will often prove useful at the commencement, and seems to render the system more obedient to the specific influence of the remedy. Should the urgent symptoms persist, notwithstanding the administration of four or five doses of quinine, or should dizziness of the head and tinnitus aurium supervene, the medicine must be discontinued; and after an interval of six or seven hours, small and repeated doses of tartarized antimony should be resorted to until full vomiting is induced. The patient should then be allowed to rest for twenty-four hours, when the quinine should be recommenced as before. If the symptoms still resist, the remedies may be repeated in succession, as above stated, for a period of four or five days."

---

* Med. Times and Gazette, 1851, p. 346.

Dr. Dundas further states that in all the stages of the disease the large doses of quinine may be safely resorted to, and will commonly calm the patient, cool his skin, allay the headache, and reduce the frequency and improve the character of the pulse.

The treatment of Dr. Dundas was adopted by Dr. Goolden and Mr. Eddowes with very favorable results.

i

Dr. Dundas in another paper * on the same subject, remarks that "Neither in my own experience, nor in that of others, so far as I am aware, have the large doses of quinine caused congestion of any important organ. On the contrary, by cutting short or moderating the febrile excitement, they prevent all such congestions, and in this consists the great value of the treatment; seeing that the vast majority of fever cases are carried off by these local affections."

Dr. Robert Gee and William Eddowes, Esq.,† medical officers of the Liverpool Fever Hospital, report very favorably of the action of large doses of quinine in typhus. These gentlemen state that "In those cases where the quinine treatment was commenced during the first seven days of the fever, the average duration of the disease was 4.4 days after the first administration of the remedy; when during the second week, 5.8 days. From cases treated during or after the third week no inference can be drawn, the disease then having nearly run its course.

"Of sixty-one uncomplicated cases, eleven were

---

* London Jour. of Med., 1851, p. 1103.

† London Lancet, 1853, p. 3.

under the treatment during the first seven days; of these, two were free from fever on the second day after treatment; one on the third day; two on the fourth day; three on the fifth day; one on the sixth day; one on the seventh day; and one on the eleventh day. In twenty-four, the treatment was commenced during the second week; of these, one was free from fever on the second day after treatment; two on the third day; five on the fourth day; seven on the fifth day; three on the sixth day; two on the seventh day; one on the eighth day; two on the ninth day; and one on the twelfth day. In twenty-six, the length of time that the fever had previously existed was not ascertained; of these, five were free from fever on the second day after treatment; six on the third day; three on the fourth day; four on the fifth day; three on the seventh day; one on the eighth day; three on the ninth day; and one on the twelfth day. The quinine was also given in twenty-seven complicated cases, the chest being involved in twenty-two, the abdomen in two, and in three both the abdomen and chest were affected; of these, twenty-two cases where the chest was involved (the affection being generally subacute bronchitis) fifteen were treated during the first week; of these, one was free from fever on the third day after treatment; one on the fourth day; two on the fifth day; four on the sixth day; two on the eighth day; one on the ninth day; two on the tenth day; one on the eleventh day; and one on the twelfth day. In seven, the treatment was commenced during the second week; of these, two were free from fever on the third day; two on the fourth day; one on the sixth day; one on the seventh day; and one on the tenth day.

"The effect of the quinine on the pulse in favorable cases was sometimes very remarkable; in one case it fell from one hundred and four to seventy-two in twenty-four hours; in another, from one hundred and forty to eighty-four in seventy-six hours; but generally speaking, the reduction is gradual and steady. In cases which terminated fatally, the quinine, with one exception, never reduced the pulse below one hundred; it sometimes fell from one hundred and forty-eight to one hundred and twenty-four; from one hundred and twelve to one hundred and eight; from one hundred and forty to one hundred and fourteen, but never below one hundred. None of the fatal cases, which were thirteen in number, were under treatment before the fifth day."

Favorable reports of the treatment of typhus with quinine have also been made by Mr. Hayward, Drs. Glassbrook, Stevenson, and others, whilst on the other hand, it has failed in the hands of Drs. Bennett, Robertson, and others. The weight of testimony certainly is in its favor, and judging from the effects of the remedy in other febrile diseases attended with cephalalgia, frequent pulse, and heat of skin, we should suppose that its employment would be attended with salutary effects. The facts sufficiently prove its sedative action on the circulation and innervation, and that it manifests no injurious effect on the secondary inflammations arising in the course of the disease. As *one* of the remedies to arrest the morbid phenomena and fatal tendencies of typhus, it certainly deserves a conspicuous position. We should expect both results if the medicine were administered in the night, in larger doses, and at intervals, for reasons previously stated.

In Erysipelas.—Cinchona was employed by Fordyce and many others in erysipelas, and soon after the discovery of the sulphate of quinine Elliotson made trials of it in the treatment of the same disease, in combination with wine and porter, in gangrenous cases. But it is not to its employment in that stage of the disease to which we wish to direct attention. It is of its use as a sedative and antiphlogistic; as a remedy possessing the power of arresting its course, that we wish more particularly to treat.

In our first experience in the treatment of erysipelas we adopted the usual method recommended by authors, and on the introduction of the tincture of the muriate of iron as a remedy for this frequently fatal malady, that valuable medicine was added to our remediate means, and employed in some cases with gratifying success. But there was a larger class of cases which this treatment did not arrest, and often signally failed in moderating in the slightest degree. These cases were marked by a very frequent, full pulse, great heat and dryness of the surface, headache, and sometimes delirium. The nervous disturbance was very conspicuously marked, and the march of the disease towards a fatal termination exceedingly rapid. Guided by a knowledge of the effects of quinine in health and disease, when freely employed, we resolved to test its powers in the first grave case presented to us.

An opportunity was soon offered, and the effects of the remedy were prompt, potent, and decided. Under its action the pulse was rapidly diminished in frequency, force, and volume; the disturbed and excited innervation was calmed, and the febrile heat quickly removed.

During the late war between the Northern and Southern States, we employed the remedy in idiopathic, and still much more frequently in traumatic, erysipelas with invariable success. Employed early in the disease, in large doses, the quantity always increased in direct ratio with the degree of fever present, the disease promptly yielded in every case. In those cases in which the disease had spent its violence before treatment, and terminated in extensive effusion and suppuration, of course we could not expect, nor did we meet with, such decided and prompt results; but even in these cases the remedy was found efficacious in arresting the further ravages of the malady, and exerted the most salutary influence in promoting recovery. In cases requiring amputation, I did not hesitate to cut through erysipelatous tissues, and found but little difficulty in checking the disease afterwards. The number of cases thus treated cannot be accurately stated, but there were three or four hundred at the least calculation.

The treatment adopted was simply to unload the bowels, if necessary, and then to administer the sulphate of quinine in doses of five to twenty grains, according to the intensity of the febrile action. On an average, thirty grains were administered in the first twelve hours; the medicine was then discontinued for twenty-four hours, and resumed if the disease continued its progress. The tincture of iron was also generally employed at the same time, and doubtless contributed greatly towards the cure. With these two remedies in the hands of the surgeon, and freely and boldly administered, I believe that erysipelas is almost as completely under control as intermittent fever.

In Scarlatina.—Morton* employed Peruvian bark in scarlet fever. In his admirable work, among others he relates the case of his own child, "*Filia mea charissima*, MARCIA," in which he employed it successfully. This disposes of all claims in regard to priority in its therapeutic use in this disease; but by a strange coincidence, before I had ever seen a copy of that old and neglected work, I used the sulphate of quinine in the case of my own child. Trusting that a brief recital of the case may prove useful, I will relate it as accurately as I can remember it. The patient was my own son, nine years of age. He was suddenly attacked with chilliness, followed by ardent fever, inflamed fauces, and well-developed eruption on the second day. The surface was of high febrile heat, except the lower extremities; these were rather below the natural temperature. The head was hot, the face flushed, and in the afternoon he became delirious and extremely restless. His bowels had been gently opened by an aperient, and at night leeches were applied to his temples, but were followed by only slight relief; these were succeeded by cold applications to the head, mustard pediluvia, etc. He continued to grow worse, and on the next night his pulse became extremely rapid, and his extremities and cheeks became decidedly cool, the delirium continuing. Knowing the property of quinine, of diffusing the animal heat, besides its sedative and calming effects, I resolved to employ it. Ten grains were administered at a dose at night. Under its operation the child fell asleep, the pulse was greatly diminished in frequency, the extremities became warm, the febrile heat of the head and body was reduced to a normal temperature, and under its subsequent use in small doses, convalescence rapidly ensued.

---

* Opera Medica, i. De Febre Scarlatina, 28–35.

I regard this case as a happy and appropriate illustration of the most valuable properties of the sulphate of quinine. Such cases are more instructive than all the experiments ever performed on dogs by M. Briquet and M. Melier, or on rabbits by M. Giacomini. We here observe the effects of a remedy in which M. Briquet, enthusiastic as he is in regard to its valuable properties, yet thinks has a tendency to produce congestion of the vessels of the pia mater. Yet in this case, in which there was as convincing proof from the symptoms that irritation and congestion of the brain existed as if it had been demonstrated by an autopsy, all the phenomena of cerebral congestion were perfectly and rapidly dissipated under its influence. It remains to those who contend that quinine excites the brain and produces congestion of its vessels to explain its therapeutic results according to their hypothesis; we give the facts. As has been forcibly said by M. Broussais, "Le vrai médecin est celui qui guérit; l'observation qui n'apprend point à guérir n'est pas

celle d'un médecin; c'est celle d'un naturaliste, ou si vous aimez mieux, d'un physiologiste ètranger au but que se propose le médecin."

Dr. Edwin A. Morrison,* of Brunswick County, Va., in an interesting article "On the Use of Quinine in Scarlet Fever," "offers to his professional brethren the benefits of his experience, sincerely trusting that those of them who may be disposed to try the prescription will find it as efficacious as it has proved to be under his direction."

This gentleman, after briefly relating some of his cases, gives the following as his mode of treatment: "When the first symptoms of the disease appear, I order quinine, regulating the dose by the age of the patient. This is administered every two or three hours until the system is brought decidedly under its influence. During this time I occasionally give a few grains of blue mass to move the bowels gently, and mop the throat with a strong solution of nitrate of silver. When the patient is old enough, I direct a gargle of red pepper tea and common salt to be used. I order the throat of a child to be washed with the same." The doctor concludes by saying, "I am aware that Peruvian bark has long ago been employed in cynanche maligna, and that some writers have maintained that this is identical with scarlet fever. Hence it may be said that there is nothing new in the use of quinine for scarlet fever. My object in this communication is not to claim originality, but to place before my medical brethren the results of my experience. I will add that my friend Dr. R. Sims, of this county, has used quinine in some few cases of scarlet fever with the happiest effect."

---

* Virginia Medical Journal, xi. 89.

In Pneumonia.—In that form of the disease assuming a periodical character of an intermittent, but usually of a remittent type, the value of the sulphate of quinine is generally conceded. Whatever the pathology of the disease may be, whether, according to the view of some writers, it is one of the numerous local congestions or inflammations occurring in the course of periodical fever and originating from the same cause, or merely an accidental complication of the pyrexial malady, the powers of the sulphate of quinine in accomplishing its cure are incontestable. An experience of forty years in regions where this form of disease is annually present enables me to add my humble but positive testimony to its capacity for not only arresting the febrile phenomena, but also the parenchymatous inflammation. It is well known to the student of malarial diseases that Morton,* J. P. Frank,† Sarcone,‡ Laennec,§ and others, had observed the wonderful powers of bark in the treatment of this disease, and that the sulphate of quinine has been found equally potent by numerous writers, but it seems to have been generally employed in reference to its supposed antiperiodic virtues; yet since its sedative and antiphlogistic action has been clearly ascertained, its effects on the inflammation have been found much more salutary. Constant || states that under the influence of large doses of quinine the hepatization rapidly disappears, and the testimony of Morehead ¶ is no less decisive. The author states that "I am not acquainted with anything more striking and satisfactory in the whole range of rational therapeutics than the progressive but

---

* Op. cit. Hist., xxi., Lugduni, 1737.

† Traité de Médecine pratique, i. 176.

‡ Maladies Observées à Naples, tome i. 176.

§ Traité de l'Auscultation mediate, 3me ed.

|| Bulletin de Thérap., xliii. 481.

¶ Clinical Researches on Disease in India, 542–43, London, 1860.

speedy restoration of a hepatized lung coexisting with fever of remittent type when the exacerbations have been controlled by the adequate use of quinine." Not only in this, but in what he considers to be idiopathic pneumonia, he gave "quinine in combination with antimony in the same manner as in the febrile cases, and very frequently with the same good effect." It is true that this author was not aware of the sedative action of quinine, and gave it as an antiperiodic, yet his therapeutic facts remain the same. In Italy, we are told by M. Briquet,* that numerous cases of pneumonia are reported as having been treated successfully by Rasori, Tommasini, and their followers, and in France by M. Favier, M. Guerard, and others.

M. Grisolle,† in his valuable work, cites a long list of authors who have used the sulphate of quinine in periodical pneumonia, and Drake‡ has recorded an equally high estimate of its virtues in the same malady. It is impossible to reconcile these proofs of the antiphlogistic and sedative effects of the sulphate of quinine with the hypothesis of its excitant and stimulant action, and whether the anatomical character of these pneumonias are congestive or inflammatory, or both, they totally disprove the conclusions of M. Melier, that the salt has any tendency to produce congestion of the parenchyma of the lungs.

---

* Op. cit., 483.

† Traité de la Pneumonie (Pneumonies periodiques), deuxieme ed., Paris, 1864, 411.

‡ Dis. Int. Valley N. A., 2d Series, 872.

To those who hold that periodical pneumonia is a hybrid disease, composed of inflammation of the lungs and remittent or intermittent fever, clinical experience affords such unanswerable proofs of the sanative effects of the quinine treatment that it must be conceded that the remedy is as efficient in removing the inflammation as it is in arresting the pyrexia.

In Cynanche Trachealis.—In ordinary croup I have witnessed the most beneficial results from the administration of the sulphate of quinine. I was first led to its employment from having often observed its remittent character, the remissions usually occurring during the morning hours. In conjunction with tartar emetic and calomel in moderate doses, I found that quinine freely employed, in doses of two to five grains, in infantile cases, materially assisted the action of those remedies, and promptly arrested the disease in the large majority of cases. I have not lost a patient with croup since I adopted this treatment.

In Delirium Tremens.—We have seen it stated that the sulphate of quinine has induced symptoms resembling delirium tremens. That this remedy may, in large doses, enfeeble the functions of the brain to such an extent as to give rise to symptoms resembling that disease, may be admitted as possible, although such an occurrence, in a very extended experience with the salt, has never been observed by me. Symptoms bearing a close resemblance often result from very different causes and conditions, but, however this may be, in *real* delirium tremens I have seen the most prompt and decided favorable results from the exhibition of quinine. To a patient laboring under this disease who had not slept for one hundred and twenty hours, and to whom large doses of laudanum and morphine had been given ineffectually, I gave twenty grains of the sulphate of quinine with the effect of producing sleep in an hour after its administration. The remedy was repeated every night in smaller doses, until perfect tranquillity of the innervation was established. Some of my professional friends have given the remedy with the ıme happy results.

In Acute Rheumatism.—Morton * gave Peruvian bark freely in acute rheumatism, not only when affecting the intermittent type, but also when presenting a continuous character; the remedy being preceded by bleeding and purgatives. This practice was likewise followed by Saunders,† Fothergill,‡ Haygarth,§ and others. Morton administered the bark in quantities of one and two ounces with prompt relief. Saunders states that he generally began "about the seventh day from the attack with the cold infusion of the red oak bark in the dose of three ounces every three hours, until the evening paroxysm came on." "I have found," he states, "in many cases by this practice, the rheumatic fever greatly shortened, and the debility and torpor in the joints, which is frequently the effect of that disease, together with the disposition to the chronic rheumatism, generally prevented." He premised the use of the bark by antiphlogistic treatment.

Haygarth at first gave the bark very cautiously in small doses, premising its administration by venesection and cathartics, but he afterwards gave it in quantities of one to two ounces in twelve hours, only preceded by an antimonial emetic. Under this treatment he stated that "the pains, sweats, and other symptoms of inflammatory fever manifestly and speedily abate till health is perfectly restored." It was his opinion that "except mercury in the syphilis, there are few or perhaps no examples where a remedy can produce such speedy relief and perfect recovery in so formidable a disease, and adds: "For many years I have been thoroughly convinced that the Peruvian bark has a much more powerful effect in the rheumatic than in any other fever; and that it does not even cure an ague so certainly and so quickly."

---

* Opera Medica, tom. i., De prot. feb. int., p. 84, et De prot. feb. cont., 149.

† Obs. on the Red Peruvian Bark, London, 1783, p. 74.

‡ Med. Observ. and Inquiries, i. 319.

§ Clinical History of Diseases, 89.

Notwithstanding these and other favorable reports of the efficacy of cinchona in rheumatism, the practice never became general, and its employment was usually limited to the last stages of the disease on account of its supposed tonic effects in relieving the exhausting sweats, etc. On the discovery of the sulphate of quinine, this remedy was also tried in the disease, but did not attract much attention until M. Briquet brought it prominently forward to the notice of the profession. This physician employed the salt in large doses in rheumatism, and in his treatise gives the history of this treatment in two hundred and fifty cases of acute and chronic forms. We translate the following extracts from his work, that give the result of his method; the effects on the circulation have been previously detailed:

"The sulphate of quinine, in doses of fifteen to forty-five and sixty grains, greatly modifies the phenomena, march, and duration of acute articular rheumatism.

"It acts as a very powerful *calmant*, and soon produces restorative *sleep*.

"The tumefactions of the joints are notably prevented; those which are already existing are diminished or lessened in their intensity. The fever which accompanies the articular lesion is also invariably diminished in a considerable degree.

"The complications of endocarditis and pericarditis did not prevent the action of the sulphate of quinine on the principal malady, but often underwent a notable amelioration from the employment of the remedy.

"When proper precaution was taken in the choice of subjects, and in the administration of the remedy, the sulphate of quinine, even in the largest doses, did not produce any serious accident."

The experience of the writer of this essay in the employment of the sulphate of quinine in acute rheumatism, although not very extensive, has been highly satisfactory. I have not, however, relied upon it solely. In plethoric subjects, the action of the remedy has always been assisted by the abstraction of blood, and in other cases by the administration of colchicum, aperients, etc. I have always found the pulse diminished in force, volume, and frequency under its use, and the violence and march of the disease controlled in an evident degree. I have seen no exasperation of the disease, or its complications, from its employment in any case. When we reflect upon the usual tedious duration of acute rheumatism, the agonizing suffering attendant upon it, and the serious organic lesions to which it so often gives rise, we should welcome any remedy which would diminish its violence and abridge its duration. That the sulphate of quinine has produced these salutary results there can be no reasonable doubt, and I feel assured that it will eventually be considered one of the most valuable additions to the therapeutics of the disease.

In Chronic Rheumatism.—The effects of the sulphate of quinine in the treatment of chronic rheumatism, though not so immediate and decisive, are generally conceded to be very beneficial. I have nothing to add on this subject to the information to be found in works generally accessible.

In Cholera Infantum.—I have witnessed the most beneficial effects from the employment of the sulphate of quinine in this disease. I was first led to use it in this fatal malady from observing the unequal distribution of animal heat to be discerned in the majority of cases, the strong tendency to congestion of the brain in the worst grades of the affection, and its simultaneous appearance and disappearance with malarial fever, etc. Given in sedative doses, I have not only seen these symptoms promptly removed, but also have generally observed the vomiting and purging to cease. I have seen it rescue cases in the last stages of the malady, when the extremities were cold and the patient in profound coma. Did the limits of this paper admit, I could relate almost miraculous recoveries from the use of the remedy in this disease in apparently hopeless conditions. In cholera infantum I usually prescribe it in doses of one to three grains (carefully watching its effects lest its sedative action might transcend the desirable degree) and repeating the doses every two or three hours, according to circumstances. In the chronic diarrhœa following attacks of cholera infantum, I usually employ it in small doses in combination with tannin and subnitrate of bismuth.

In Cerebro-Spinal Meningitis.—I have, save in a single case, invariably used quinine in large doses in the treatment of this disease, and with the most satisfactory results. Only one death has occurred in my practice, and in that NO *quinine was given.* That case was of the *fulminant* form,—the *méningite foudroyante* of the French,—in which death occurred in twelve hours from the commencement of the attack. The patient was seized with symptoms resembling a chill at 8 A.M.; tardy and imperfect reaction ensued; the head was hot and the body warm, but the extremities continued cool to the last. Comatose delirium and opisthotonos occurred at one o'clock P.M., only five hours after the invasion, the pulse remaining feeble, frequent, and contracted from the commencement. I was convinced from the rapid course and grave symptoms of this case that there was no remedy known that offered a hope of salvation in such conditions except quinine. In the cases afterwards treated, the patients were promptly purged with free doses of calomel (ten to twenty grains), and quinine was simultaneously or soon after administered in doses of fifteen to twenty grains. Relief of pain and sleep were further secured by full doses of hydrate of chloral (ten to fifteen grains), given every two to four hours, with prompt blistering over the occipital region. The administration of quinine was regulated by the thermometer,—increasing or diminishing the dose *pari passu* with the rise and fall of the internal temperature. Under this treatment, prolonged sleep and relaxation of the spinal tetanic spasm occurred; profuse blackish-green discharges from the bowels appeared, and when awaking the mind cleared up, and gradual, but certain and regular, convalescence ensued.

Now, what is the pathological anatomy of this disease? Indisputable appearances of intense inflammation of the pia mater investing both brain and spinal marrow, congestion of the substance of the brain and medulla spinalis, copious effusions of serum in the cerebro-spinal cavities, and frequently the abundant presence of pus itself. Let us not forget that similar appearances of cerebro-spinal inflammation were present in the cases of the delirious form of periodical fever, described by Torti, Senac, Lind, Hildenbrand, Bailly, Maillot, Gintrac, Nepple, Morehead, Berenguier, Monfalcon, Mongellaz, and others, in all of which cinchona or quinine was found to be the only reliable remedy, and we must be convinced that quinine, so far from producing congestion or exciting inflammation of the brain, has proven itself to be one of the most certain remedies in removing those lesions in a vast number of cases.

In Surgical Shock.—In the *Virginia Medical Monthly* of August, 1878, Dr. Hunter McGuire, of Richmond, Va., suggested the use of quinine to lessen or prevent shock following surgical operations, etc. Dr. McGuire's experience has been confirmed by that of other surgeons, and quinine is now frequently given to patients who are about to undergo serious surgical operations. This distinguished surgeon recommends that on the morning of the day of operation five grains of the sulphate should be given every two hours until slight but decided symptoms of cinchonism are produced.

In many cases of railway injuries, burns, etc., in which the symptoms of shock were extremely grave, Dr. McGuire has employed quinine by the mouth and hypodermically with decided benefit.

MODUS OPERANDI OF QUININE.

It must be confessed that the mode by which remedies counteract and remove disease is a subject replete with difficulty and obscurity. The phenomena of disease—perverted life—can never be perfectly explained until the science of normal life is clearly understood, but as there are many ascertained truths in physiology, we often arrive at an approximate knowledge of the action of remedies, and are thereby enabled to formulate instructive classifications and to institute safe and reliable rules in regard to their use and action. Let us, then, with the lights before us, endeavor to ascertain the *modus operandi* of the most certain and valuable remedy yet discovered.

It is a source of just pride with therapeutists that in quinine they possess a sure and reliable agent for the cure of wide-spread and too often fatal diseases. The diminution of the mortality in malarial regions since its introduction has been so evident and incontestable, that it has engaged the attention of all civilized nations and has received the earnest consideration of the highest departments of government. It is, therefore, a matter of great moment to ascertain its method of operation, as it may lead to a better understanding of the essential nature of disease, open the way to the discovery of other agents possessing similar or substitutive powers, and enable us to discover the recondite connection between the various and apparently dissimilar maladies in whose treatment its employment has been found to be universally efficacious.

As we have seen, the first effect of quinine on the human economy is made evident by an altered function of a nerve of special sense, viz., the auditory nerve. This is often produced in susceptible subjects by minute doses of the agent, and consists of varying degrees of tinnitus aurium and deafness. Subsequently, whether the salt is given in large doses, or after the repetition of small doses, we observe a certain and gradual reduction of heat, relief of cerebro-spinal pain, mitigation and disappearance of restlessness, decline of the pulse in force, frequency and volume, cessation of nausea and vomiting, copious diuresis and diaphoresis, psychical calm and normal-like sleep. If the dose of the medicine be further increased, the patient complains of dimness of vision, confusion of thought, and vertiginous sensations. He then becomes indifferent to all surrounding objects. He desires nothing, hopes for nothing, fears nothing. Although he may be easily aroused, and his replies are intelligible and reasonable, he soon relapses into delightful slumber. The remedy pushed further, the pulse gives way, becoming feeble, small, and frequent, the skin becomes cool or cold and bathed in a copious, adhesive perspiration, the patient becomes blind, perfectly deaf, and comatose, and in rare instances death closes the scene. It will be seen, therefore, that the primary impression of the medicine is made upon that portion of the medulla oblongata from which the auditory nerve arises, the posterior root of which may be traced to the gray matter beneath the floor of the fourth ventricle, which is connected with the white substance of the cerebellum, the anterior roots springing from the borders of the calamus scriptorius, and some of its fibres also being traced to the cerebellum. We are thus enabled to map out a small space in the nervous centres, from which the auditory nerve takes its origin,—the hyperæsthesial region in quinial intoxication.

Again, the dimness of vision experienced by some patients can only be attributed to the action of the salt upon the origins of the optic tracts, viz., the corpora quadrigemina, corpora geniculata, and optic thalami, whilst if the medicine be pushed further, its effects are proven not only by its relief of pain in the cerebro-spinal and ganglionic systems, but also by the induction of sleep, due to its action on the gray matter of the cerebral convolutions.

Let us now examine into the pathology of malarial poisoning, against which it is universally recognized as the most potent remedy.

It may be regarded as a self-evident proposition that malaria is a *materies morbi*, which being absorbed by the blood and conveyed throughout the system, manifests a special affinity for the nervous system. As we have said, this is proven by the vast number of cases of neuralgia of a strictly periodical character, involving every nerve in both systems of nerves and every part of their centres, and giving rise not only to pain, but to disordered function and various lesions in the parts to which those nerves are distributed. These phenomena can only be due to the influence of an irritant poison ing in the blood and impinging upon those of the nervous system most readily impressible by the noxious agent. It is then upon IMPRESSIBILITY of the nervous centres, and especially of the cerebro-spinal system, that quinine exerts its influence. It obtunds, stupefies the impressionable centre, and renders the action of the poison ineffectual. Why any poison should select special parts of the nervous centres for its toxic invasion we cannot explain, but it is proven by observation of the effects of many poisons. Need we point to the innumerable localizations of the syphilitic poison as a familiar example, which are all mitigated or removed by the same remedial agents? That this theory, that quinine exerts its remediate power by rendering the nervous centres insensible or unimpressible, is true is further supported by the fact that other agents which have been proven to be remediate in malarial fever possess, in common with it, the power of impairing or even destroying the impressibility of the nervous centres. The reputation that opium for centuries enjoyed, and later the effects of chloroform in the treatment of malarial poisoning, are doubtless due to their analogous effects on the centres of impressibility.

It is well known to those who have had extensive experience in cases of malarial poisoning, that many cases are self-limited in their duration, and terminate in health without remediate measures,—the poison being spontaneously eliminated from the system. Quinine would then reasonably seem to cure, or at least to obviate the pernicious effects of the poison, by rendering the centres of impressibility insensible to its action while under its paralyzing influence, and thus affording time for the noxious agent to be eliminated from the system. The great tendency to relapse in such affections, even in those cases in which the system had been saturated with the medicine, seems to prove that its therapeutic effects are not due to any antidotal or germicidal property. The morbid phenomena return after the centres have escaped from the stupefying, or we may say the partially paralyzing effect of quinine. It is generally supposed by those who have never resided in regions where the malarial poison is most concentrated and malignant in its character, that the inhabitants universally suffer from the influence of the poison. It is true that a vast *number do* suffer from its toxical impression, but it is as equally true that a very large number *do not suffer* at all, and preserve their health intact in the poisonous atmosphere. They enjoy an *immunity* either partial or perfect, transitory or permanent, against the power of the poison, and why? It cannot be denied but they also absorb the poison into the blood. In the air they all breathe, the deadly agent floats; in the waters they drink, as Hippocrates held, the mortal miasm is held in solution; from the soil they till, the hidden foe starts up. How can we explain this immunity save by the facts that the impressibility is not aroused; that the sensibility of the nervous centres does not respond to nor is affected by the poison absorbed by the blood and circulating through the substance of its tissues, in the same manner as they are not affected by many other poisons proven to be present in the blood? The first taste of tobacco sickens with unendurable nausea; the first drink of brandy intoxicates to madness and coma; the first dose of opium paralyzes the senses, destroys the consciousness, and poisons the centres of both systems; but by habitual use the *impressibility* to these is lost, and the same agent that poisoned before is now unfelt and innocuous. The poison is still absorbed in the blood, but the centres do not respond; the *power* of *impressing* is in *abeyance*, because they are no *longer capable of being impressed.*

Quinine, therefore, confers *immunity* from the effects of the *toxic* agent by *obtunding*, *stupefying*, and even *paralyzing* the centres of impressibility, and, therefore, so far as the patient is concerned, placing him on the same plane as his healthy comrade, who, exposed to the same cause, is inhaling and absorbing the same poison, which, though circulating throughout his entire being and permeating every living tissue, is as harmless as the mother's normal milk to the healthy infant.

All of the secondary phenomena arising from the action of the malarial poison—pain, fever, perverted sensations, and impaired function—are evidently due to disturbance of special centres, which cease as if by enchantment as soon as the impressibility of those centres is sufficiently impaired or suspended.

It is well known to the scholar that malaria may concentrate its action upon any part of the nervous system, and there is every reason to believe that it thereby perverts the functions of every part to which their nerves are distributed,—*neuralgia of every nerve*, *congestion*, *irritation*, *inflammation of every organ*, *and fever of every type*, may be the consequence of its malign influence; yet all these various pathological conditions yield to the same remedy. In like manner, its beneficial effects in many other diseases may be explained. It impairs or suspends the impressibility of the sources of innervation, and gives time for the elimination from the organism of the various morbific agents from which they originate. We cannot otherwise explain the salutary action of quinine in diseases arising from entirely different causes, as, for example, malarial fever, cerebro-spinal meningitis, rheumatism, erysipelas, etc., in which its virtues have been attested by so many distinguished authorities.

In the absence of any other satisfactory solution of the *modus operandi* of quinine, we are justified in declaring that it potently contributes to the removal of disease by rendering the nervous system insensible to the action of the morbific causes of those maladies in which its employment has been proven by experience to be efficacious. It does not, to use a hackneyed phrase, *inhibit reflex action*, for reflex action requires as its factors an afferent nerve, a sensitive centre, and an efferent conductor of a reflected impression, but it *impairs the impressibility itself*, and "fatal things pass harmless" by the paralyzed centre. The centre does not and cannot reflect an impression which it has been rendered incapable of receiving. It has been *paralyzed partially or perfectly* by quinine, and therefore placed beyond the pale of danger. In a word, if we may be excused for coining a new term, *quinine is a* PARALYSANT. This may seem a severe and repulsive designation, as in proper quantities it merely *benumbs, stupefies, or narcotizes* the nervous centres, but these really are but *varying degrees* of PARESIS. The *theory* here advanced, based solely on *facts*, can only lead to *safe* and *certain results* if guided by the inexorable rule in its administration *the physician constantly has in view the end to be attained*, viz., to render the receptive centres securely insentient to its morbific assailants, and to hold them in subjection until they have lost, by elimination or from exhaustion, their power to impress. This can only be accomplished by increasing the quantity of the remedy until the desired effect is secured. If, as happens in rare instances, its depressing effects should transcend the normal degree, they may be speedily removed by the moderate use of brandy or other alcoholic stimuli.

MODE OF ADMINISTRATION.

The sulphate of quinine may be administered in various modes. When given by the mouth, we prefer to administer it simply diffused in water or in pills freshly made with syrup of gum acacia, or made into a pilular mass and placed in gelatine capsules. By the latter mode, the patient is relieved from its bitter taste, and we have always found it as efficacious as when given in solution. In cases of intense gastric irritability, immediate danger, or in those in which patients are unable to swallow, as sometimes happens in malignant forms of fever, it may be administered by the rectum, usually an excellent and efficient method, or injected beneath the skin. From numerous trials of the hypodermic method, its effects have been found to be prompt and efficient. For this purpose, the formula of M. Dodeuil, already given (page 109), may be used, or the salt may be dissolved in recently distilled water, by the addition of a few drops of dilute sulphuric acid. These methods of administering the remedy render its employment by other and more uncertain practices of applying it to blistered surfaces, etc., entirely unnecessary. When introduced by the rectum, it should be given in at least double the quantity of the ordinary dose, and in the case of children, when given by the mouth, it may be disguised in coffee, milk, or licorice.

In conclusion, I feel that I should be doing injustice to others, as well as myself, if I neglected to add that in the numerous trials and experiments I have made with the sulphate of quinine during the last forty years, I have generally used that formerly prepared by John Farr, and since by his worthy successors, Powers & Weightman, of Philadelphia. Many adulterated and spurious articles have been offered for sale in our markets, but the product of the above establishment has never failed in my hands to accomplish the desired result. I therefore desire to record my thanks to this house of honest chemists for having furnished to the world a pure preparation by which thousands of lives have been saved.

Works of Reference and Dictionaries.

S. Austin Allibone.

Dictionary of English Literature, and British and American Authors. 3 vols. Royal 8vo, extra cloth, $22.50.

Prose Quotations, from Socrates to Macaulay. 8vo, cloth, $4.50.

Dictionary of Poetical Quotations, from the Time of Chaucer to the Present Day. 8vo, cloth, $4.50.

Great Authors of All Ages. 8vo, cloth, $4.50.

John Bouvier.

Law Dictionary. 2 vols. 8vo, law sheep, $12.00.

Law Institutes. 2 vols. 8vo, law sheep, $12.00.

A. and G. Biddle.

The Law of Stock Brokers. Crown 8vo, sheep, $5.00.

E. Brewer, LL.D.

The Reader's Hand-Book. 12mo, half morocco, $3.50.

Chambers.

Book of Days. Illustrated. 2 vols. Royal 8vo, cloth, $8.00.

Cyclopædia of English Literature. 2 vols. Royal 8vo, cloth, $8.00.

Encyclopædia. *Popular Edition, Revised.* In ten 8vo volumes, with 4000 Engravings and 40 Maps. Per set, cloth, $25.00.

Household Edition, Revised. 10 vols. Same as above except the maps, and printed on thinner paper. Cloth, $15.00.

Information for the People. 2 vols. Royal 8vo, cloth, $7.00.

Contanseau.

Dictionary of the French and English Languages. Crown 8vo, cloth, $2.50.

E. Edwards.

Words, Facts, and Phrases. 12mo, half morocco, $2.50; half Russia, $4.00.

Encyclopædia of Chemistry.

2 vols. Per vol.. cloth, $12.00.*

Lempriere.

Classical Dictionary. 8vo, sheep, $3.25.*

Leverett.

Latin Lexicon. 8vo, sheep, $3.50.*

Sharswood.

Blackstone's Commentaries on the Laws of England. 2 vols. 8vo, $10.00.*

Lippincott's Dictionary of Biography.

Edited by J. Thomas, M.D. Royal 8vo, complete in 1 vol. Sheep, library style, $10.00.*

The Same. 2 vols. Per set, extra cloth, bevelled boards, $18.00.

Lippincott's Gazetteer of the World.

New Edition. Thoroughly Revised, Rewritten, and Enlarged. Imperial octavo, library sheep, $10.00.*

Longman.

Pocket Dictionary of the German and English Languages. 18mo, cloth, $1.50.

Worcester.

Standard Royal Quarto Dictionary of the English Language. *New Edition,* with Supplement, containing 12,500 New Words. Sheep, marbled edges, $10.00.*

Washington Irving.

The Sketch Book. Illustrated. *Cabinet Edition.* Quarto, fine tinted paper, cloth extra, $4.50.
The Artist's Edition. Quarto, cloth, gilt, $7.00.

Jenkin.

Vest-Pocket Lexicon. 64mo, roan, gilt edges, 75 cents.

Col. T. T. S. Laidley.

A Course of Instructions in Rifle Firing. 16mo, cloth, $1.50.*

G. N. Lamphere.

The United States Government. 8vo, cloth, $2.50.

L. L. Langstroth.

Practical Treatise on the Hive and Honey Bee. 12mo, cloth, $2.00.

E. J. Lewis, M.D.

The American Sportsman. 8vo, cloth, $2.25.

F. Lieber, LL.D.

On Civil Liberty and Self-Government. Edited by Theodore D. Woolsey. 8vo, cloth, $3.15.*
Political Ethics. Edited by Theodore D. Woolsey. 2 vols. 8vo, cloth, $5.50.*
Miscellaneous Writings. 2 vols. 8vo, cloth, $6.00.

Edward Mayhew, M.R.C.V.S.

Illustrated Horse Management. 8vo, cloth, $3.00.
The Illustrated Horse Doctor. 8vo, cloth, $3.00.

L. P. Meredith.

Everyday Errors of Speech. 16mo, cloth limp, 75 cents.

F. L. Oswald.

Summerland Sketches. Illustrated. 8vo, cloth, $3.00.

Elizabeth Peake.

Pen Pictures of Europe. Illustrated. Crown 8vo, cloth, $3.50.

History of the German Emperors. Illustrated. 8vo, cloth, $3.00.

Philosophical Classics for English Readers.

Edited by William Knight, LL.D. 12mo, per vol., cloth, $1.25.

Now Ready.

Descartes. By Prof. Mahaffy.
Butler. By Rev. W. L. Collins.
Berkeley. By Prof. Fraser.
Fichte. By Prof. Adamson.
Hume. By Wm. Knight, LL.D.

Major Serpa Pinto.

How I Crossed Africa. Illustrated. 2 vols. 8vo, $7.00.

Quotations.

Ancient and Modern Familiar Quotations. Crown 8vo, cloth, $2.00.

Schiller.

Works. 6 vols. 12mo, extra cloth, $9.00.

James R. Snowden.

Manual of Coins. 8vo, cloth, $6.00.

Rev. C. H. Spurgeon.

John Ploughman's Pictures. 16mo, cloth, $1.00.

LANE MEDICAL LIBRARY

To avoid fine, this book should be returned on or before the date last stamped below.

JUL 23 1930		

U666 Manson, O.F. 14833
C53M2 Sulphate of quinine.
1882

NAME	DATE DUE
M. Cochran	[illegible]